Special tube? NO

reaction volume and tube time constant data. This curve will be used to extrapolate the correct Tau (tube time constant) for each run using this special tube depending on the reaction volume entered by the user at the start of a run.

UTIL - USER CONFIGURATION (cont)

Rxn vol=xxxuL T=xxxs Rxn vol=xxxuL T=xxxs

3 sets of this screen will be offered if the user sets "Special tube?" to YES.

EPNSDOCID: <EP___0810030A1_I_>

UTIL - DELETE

Delete PROGRAM-USER-ALL	

Delete by PROGRAM

Delete Enter program #xxx	All programs (files and methods) can be deleted by number.
Can't delete progxxx Linked in methodxxx!	A program cannot be deleted if it linked in a method.
Progxxx is protected Enter user #xxxx	The user has entered the # of a protected program. The correct user # must be entered in order to delete this program.
Progxxx is protected Wrong user number!	The wrong user # was entered. This display remains for 5 seconds before reverting to the previous one. The user is given 3 chances to enter the correct #.
Prog #xxx User #xxxx Delete program? YES	Ready to delete the program. The user # appears only if the program was protected.

Delete by USER

Delete Enter user #xxxx	Programs can be deleted under a given user number.
Delete No progs with #xxxx	If no programs exist with the given user #, the following message is displayed.

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Progs linked in meth STEP to list progs	Programs cannot be deleted if they are linked in a method. The STEP key will cycle through the list of linked programs.

UTIL - DELETE (cont)

Can't delete progxxx Linked in methodxxx!	The list of the linked programs will show which method the program is linked to.
User #xxxx Delete all progs?YES	This will delete all the programs under the given user # that are not linked.

Delete ALL

Delete every unprotected prog?YES	This will delete every unprotected program that is not linked in a protected method.

BNSDOCID: <EP___0810030A1_I_>

UTIL - USER DIAGNOSTICS

While running any diagnostic t st, the STOP key always returns the user to the top l vel diagnostic screen and automatically increments the test number and name to the next test. This facilitates manually cycling through the available diagnostics.

```
Enter Diag Test #1
REVIEW HISTORY FILE
```

The user can enter the number of the diagnostic to run or can use the STEP or BACK keys to cycle through the available tests. Every time the STEP or BACK key is pressed, the test number is incremented or decremented and the associated test name is displayed. This feature eliminates the need for the user to memorize the number associated with each test.

REVIEW HISTORY FILE

```
Enter Diag Test #1
REVIEW HISTORY FILE
```

The history file is a circular buffer in battery RAM which can store up to 500 records of the latest run. When the buffer is full, the oldest entries will be overwritten. The buffer will automatically be cleared before a program is executed.

```
HISTORY      nnn recs
ALL-STAT-ERRORS-PRNT
```

The history file header displays the current number of records in the file ('nnn').
ALL views all the records
STAT views only the status records
ERRORS views only the records with error messages
PRNT prints all or part of the history file

The two types of records are 1) status records which give information about the program and 2) data records which give information abount each hold and ramp segment in a program. A Hold program is treated as one hold segment and the data record will be stored when the file ends.

Since there could be hundreds of entries (50 cycles X 6 setpoints ~= 350 entries), fast, bi-directional movement through the file is required. Note that most PCR programs will be 3 or 6 setpoints and 40 cycles or less. The entries will normally be reviewed in reverse order, thus the first

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record seen will be the last record written.

If the user has chosen a type of record to view, STEP or BACK will move down or up the buffer by one entry of the chosen type. By preceding STEP or BACK with a number, the second line is replaced with "Skip #XXX entries". The user enters a number and presses ENTER to accept the value and that number of entries is skipped going forward (STEP) or backward (BACK).

By preceding STEP or BACK with the RUN key, the user can quickly move to the largest record # (the newest record) or record #1 (the oldest record) of the chosen type.

STOP terminates the review mode and displays the file header.

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STATUS RECORD

ffff #xxx/mmm nnn message

'ffff' is either HOLD, CYCL or AUTO
'xxx' is the program number
'/mmm' is the method number for a linked program, else blank
'nnn' is the record number
'message' is one of the following:

Status messages

Tube Type: xxxxx	Type of sample tube used in the run
Reaction vol: xxxuL	Reaction volume used in the run
Clk starts w/in x.xC	The hold clock starts within this temp of setpoint
Start xx/xx/xx xx:xx	Time and date of the start of the run
End xx/xx/xx xx:xx	Time and date of the end of the run
Meth Complete	All programs linked in the method are complete
Pause xx:xx at xx.xC	The program paused for this time at this temp

Fatal status messages

Sensor Error	A sensor had a bad reading 10 times in a row
Power fail xxx.x hrs	The power was off for this amount of time
User Abort	The user pressed the STOP key during the run
Pause Timeout xx:xx	The keypad pause has reached its configurable time limit.
Fatal Setpoint Error	Is the requirement to abort a program if the setpoint is not reached within a calculated amount of time. A 10 X 10 lookup table of starting ramp temperature (0°C - 100°C in 10°C increments) vs. ending ramp temperature (same axis labeling) will hold the average time the TC2 should take to ramp up or down any given amount of degrees. The file will be aborted if the setpoint is not reached in the amount of time calculated as follows:

programmed ramp time + (2 * lookup table value) + 10 minutes

DATA RECORD

'f' is either HOLD, CYCL or AUTO
'xxx' is the program number

BNSDOCID: <EP___0810030A1_I_>

f#xxx/mmm ddd.dC nnn Cycyy Setpt z mmm:ss

'/mmm' is the method number for a linked program else blank
'ddd.d' is the ending setpoint temp
'nnn' is the record number
'yy' is the cycle number
'z' is the setpoint number
'mmm:ss' is the setpoint time

The cycle and setpoint number fields will be omitted for a Hold program.

DATA ERROR RECORD

message ddd.dC nnn Cycyy Setpt z mmm:ss

'ddd.d' is the ending setpoint temp
'nnn' is the record number
'yy' is the cycle number
'z' is the setpoint number
'mmm:ss' is the setpoint time
'message' indicates a non-fatal error as follows:

Non-fatal Error messages

Setp Error The setpoint was not reached in the calculated time:
programmed ramp time + (2 * lookup table value).

Prog Error An Auto program auto increment/decrement of the setpoint temp or time caused the hold time to go negative or the temp to go out of the range 0.1°C to 100°C.

Temp Error At the end of the segment, the setpoint temp has drifted +/- a user configurable amount.

For the Hold program, the cycle and setpoint fields will be omitted.

BNSDOCID: <EP___0810030A1_I_>

PRINTING THE HISTORY FILE

Access to the history fil print routines is through the history file header menu. The OPTION key cycles the cursor through the options:

```
HISTORY      nnn recs
ALL-STAT-ERRORS-PRNT
```

Pressing the ENTER key when the cursor is positioned under PRNT displays the print screen:

```
Print History
ALL-STAT-ERRORS
```

ALL	prints all the records in the file
STAT	prints only the status records
ERRORS	prints only the records with error messages

When one of print options is selected, the following screen is displayed:

```
Print History
Print from prog #xx
```

The first (most recent) program number will be the default program. The user can change the program number from which to begin printing. While printing, the following screen is displayed:

```
Print History
...printing
```

At the end of printing, the Print History menu is again displayed.

BNSDOCID: <EP___0810030A1_I_>

HEATER TEST

```
Enter Diag Test #2
HEATER TEST
```

The heater test calculates the heat rate of the sample block as its temperature rises from 35°C to 65°C. The following screen is displayed as it forces the block temperature to 35°C.

```
Heater Test Blk=XX.X
going to 35C...
```

When the temperature stabilizes, all heaters are turned on full power. The display now reads "going to 65C" and the block temperature is monitored for 20 seconds after it passes 50°C. After 20 seconds, a pass or fail message is displayed.

```
Heater Test PASSES
```


BNSDOCID: <EP___0810030A1_I_>

CHILLER TEST

```
Enter Diag Test #3
CHILLER TEST
```

The chiller test calculates the cool rate of the sample block as its temperature drops from 35°C to 15°C. The following screen is displayed as it forces the block temperature to 35°C.

```
Chillr Test Blk=XX.X
going to 35C...
```

When the temperature stabilizes, the chiller is on. The display now reads "going to 15C" and the block temperature is monitored for 20 seconds after it passes 25°C. After 20 seconds, a pass or fail message is displayed.

```
Chiller test PASSES
```

Claims

1. A thermocycler apparatus suitable for performing the polymerase chain reaction comprising

   a metal sample block having an array of spaced-apart sample wells each of which has an inside surface, said wells being provided with one or more capped sample tubes each containing a sample mixture placed in a microtiter plate having an uppermost edge, which plate is seated on said sample block, and

   a cover to enclose said capped sample tubes, which cover comprises a flat, horizontal rectangular portion and downwardly projecting skirt portions along the periphery thereof and further comprises a device for heating at least the underside of said horizontal portion, said cover being dimensioned to contact said sample block and to enclose said microtiter plate and capped sample tubes on said sample block when the tops of the caps on said sample tubes deform, due to the application of heat and a downwardly directed force on said cover.

2. Apparatus as claimed in claim 1, wherein said side portions of the cover are dimensioned such that said skirt portions contact said sample block at substantially the same time as the underside of said cover contacts the uppermost edge of said microtiter plate as the cover encloses the plate, preferably wherein the downwardly directed force is sufficient to ensure a snug contact between a lower portion of each sample tube and the inside surface of the well which contains said portion.

3. Apparatus as claimed in claim 1 or claim 2 further comprising knob and screw means for lowering said cover from one height to another, said knob and screw means including indication means for identifying a knob position corresponding to the cover height at which said cover contacts said uppermost edge.

4. Apparatus as claimed in any one of claims 1 to 3, wherein said cover provides sufficient heating to said capped sample tubes so as to heat the caps and the portions of the sample tubes positioned above the sample wells to a temperature above a condensation point of vapour from the sample mixture in said one or more tubes.

BNSDOCID: <EP___0810030A1_I_>

5. A thermocycler apparatus suitable for performing the polymerase chain reaction comprising a sample well capable of receiving at least one capped plastic sample tube Containing a sample mixture, and a heated cover for said at least one sample tube.

6. A disposable reaction container comprising a substantially conically shaped first wall portion and a substantially cylindrically shaped second wall portion, said first wall portion being adapted to contact along substantially its entire outer surface a correspondingly shaped portion of a heat exchanger, said first wall portion being substantially thinner in wall cross-section than said second wall portion.

7. A container as claimed in claim 6 which is adapted to receive a cap which forms a gas-tight seal when engaged over said cylindrically shaped second wall portion.

8. A container as claimed in claim 6 or claim 7, wherein the angle defined by the longitudinal axis through said reaction container and the substantially conically shaped first wall portion is about 17°, preferably said first wall portion is from about 0.009 to about 0.012 inches in wall cross-section, and/or said second wall portion is about 0.030 inches in wall cross-section.

9. A container as claimed in any one of claims 6 to 8 which is made from an autoclavable plastic, preferably polypropylene.

10. A container as claimed in any one of claims 6 to 9 additionally comprising a cap which is connected by a web to the reaction container and which is capable of forming a gas-tight seal with the upper portion of said second wall portion, preferably said container has sufficient strength to withstand the application of a downward force to said cap when said cap is in place atop the upper portion of said second wall portion, which force is applied so as to deform said cap.

11. A container as claimed in any one of claims 6 to 10 which additionally comprises an annular flange which extends outwardly from the outside of said second wall portion.

BNSDOCID: <EP___0810030A1_I_>

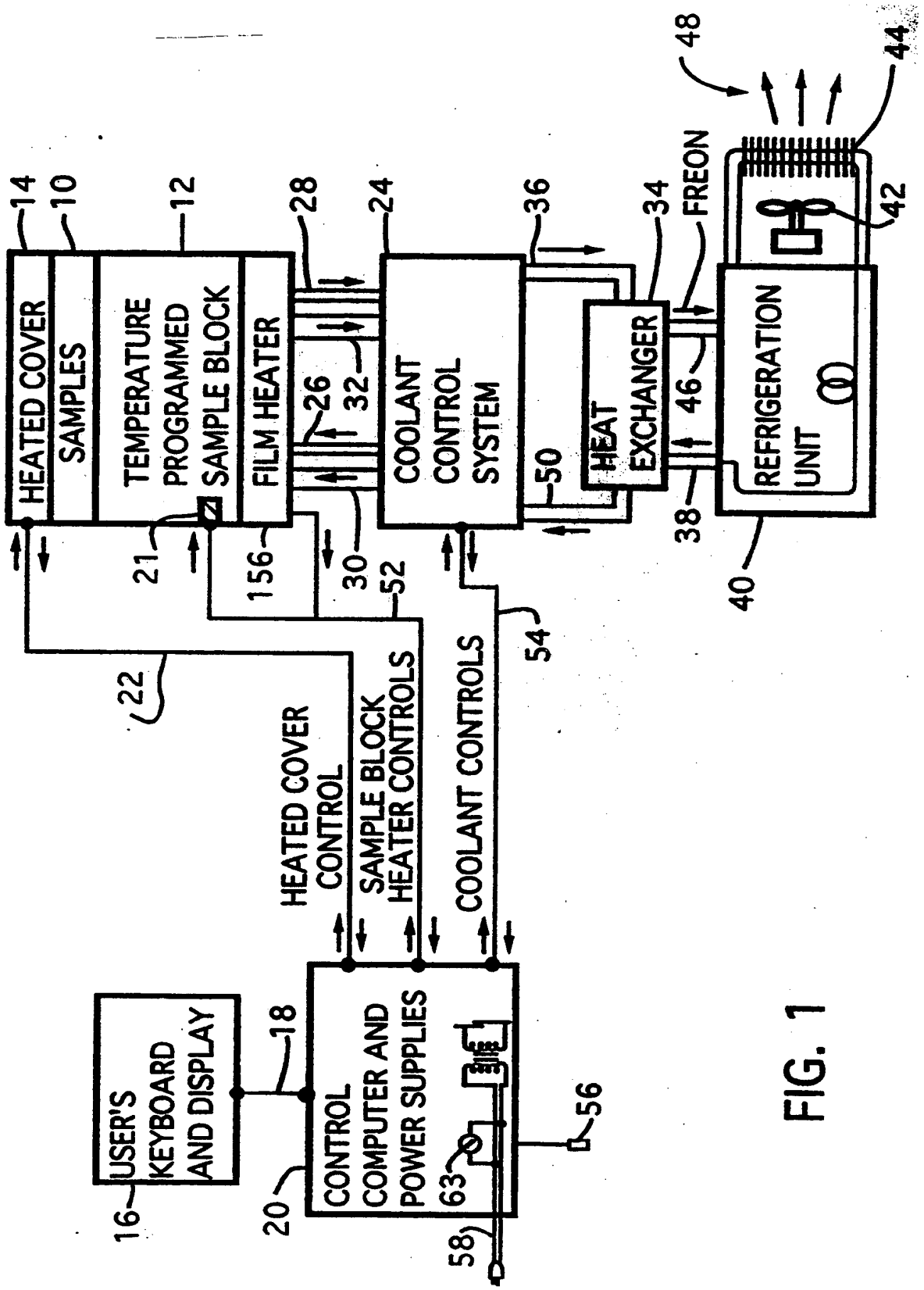

FIG. 1

BNSDOCID: <EP___0810030A1_I_>

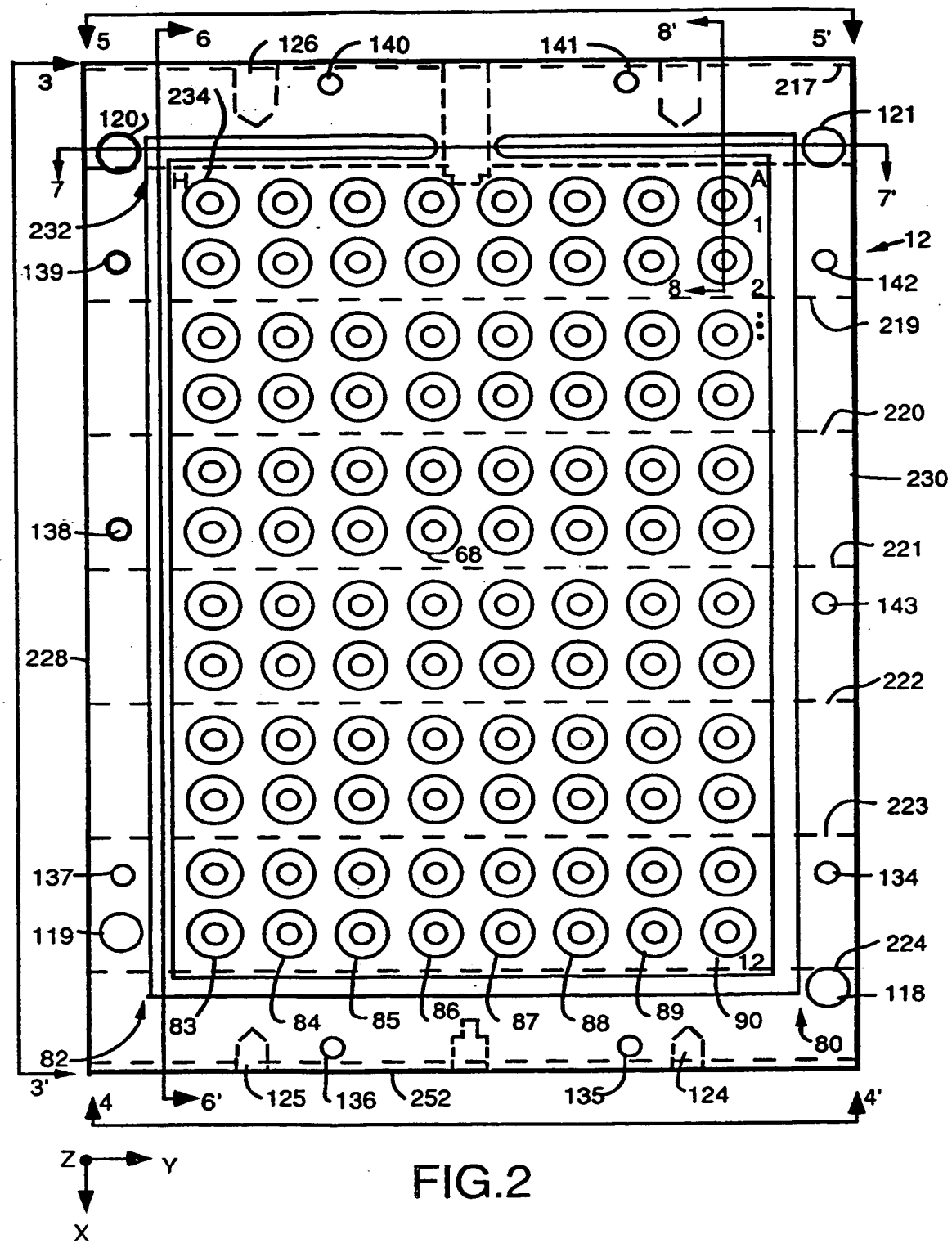

FIG.2

BNSDOCID: <EP___0810030A1_I_>

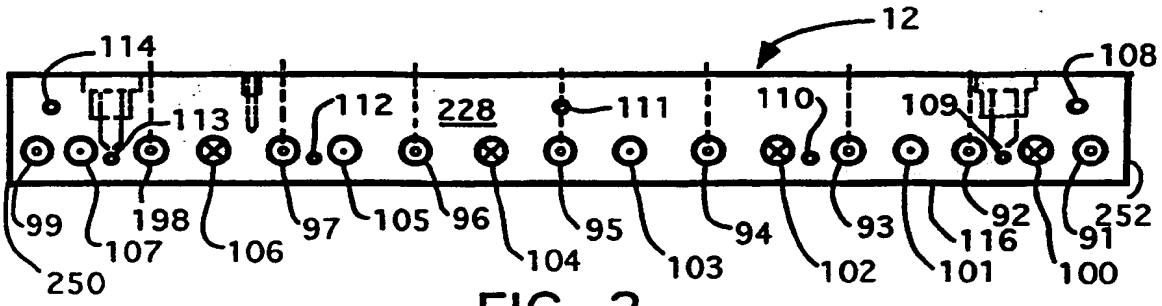

FIG. 3

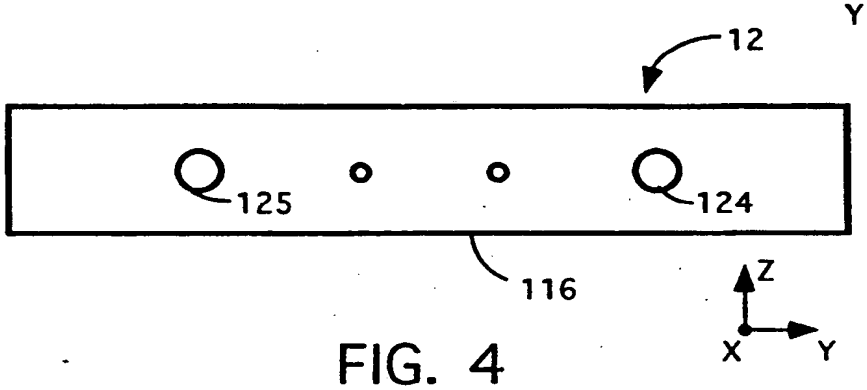

FIG. 4

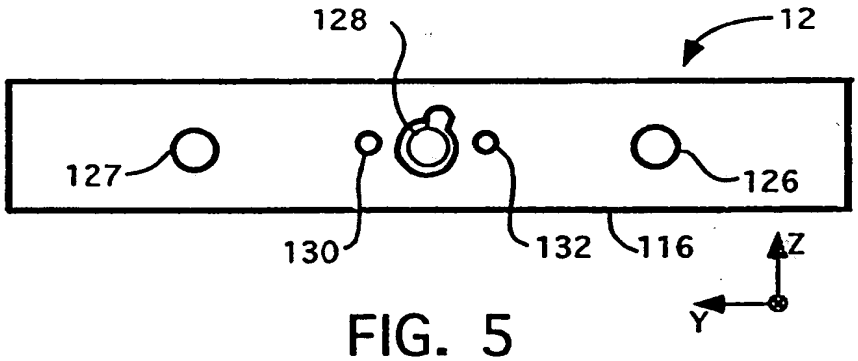

FIG. 5

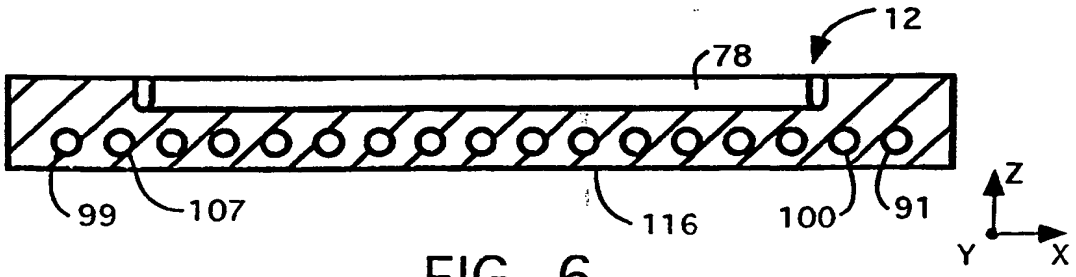

FIG. 6

BNSDOCID: <EP___0810030A1_I_>

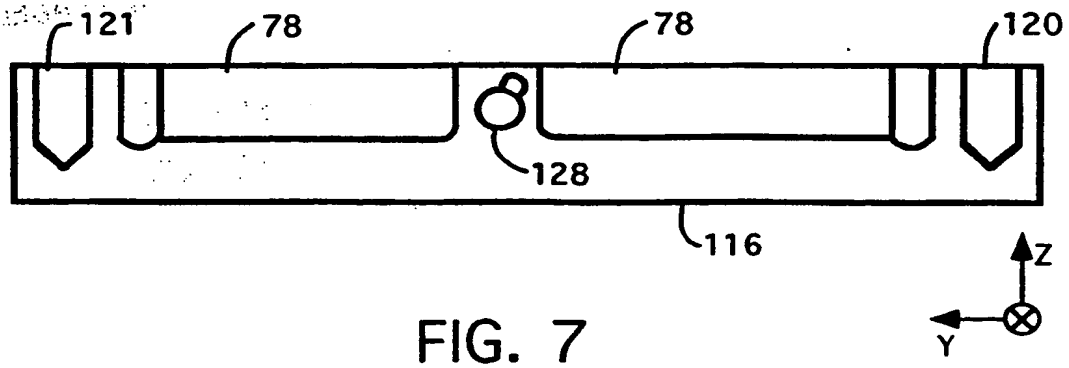

FIG. 7

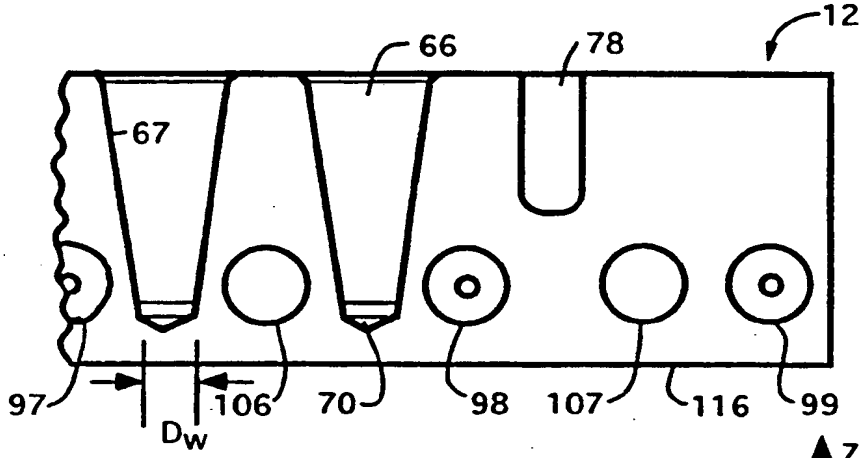

FIG. 8

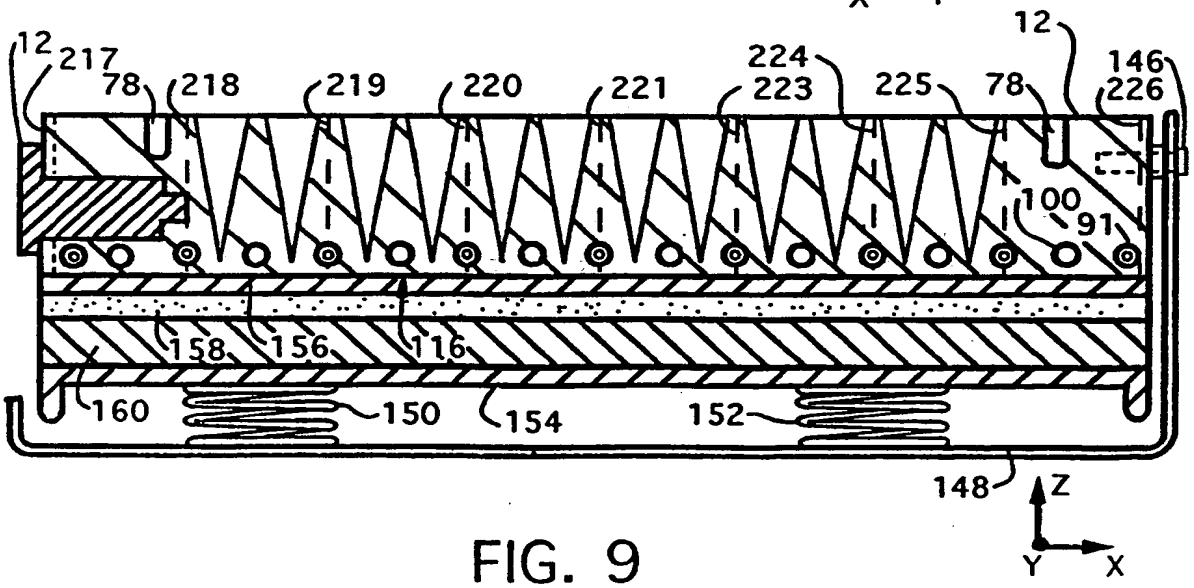

FIG. 9

BNSDOCID: <EP___0810030A1_I_>

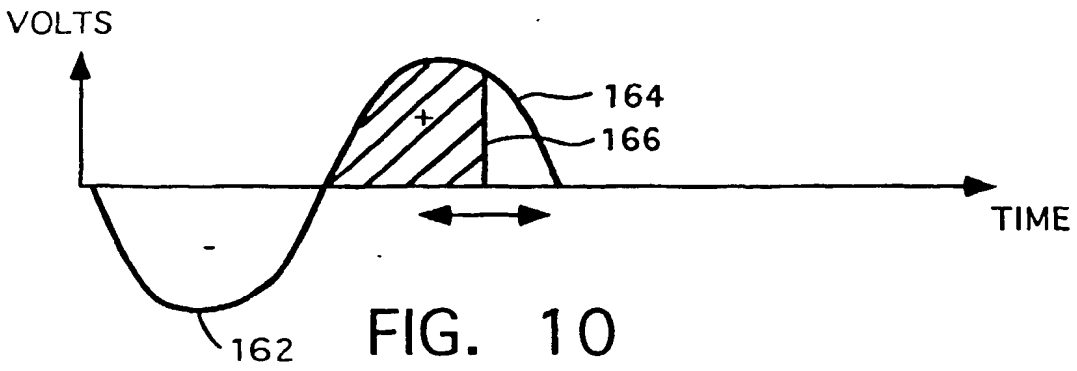

FIG. 10

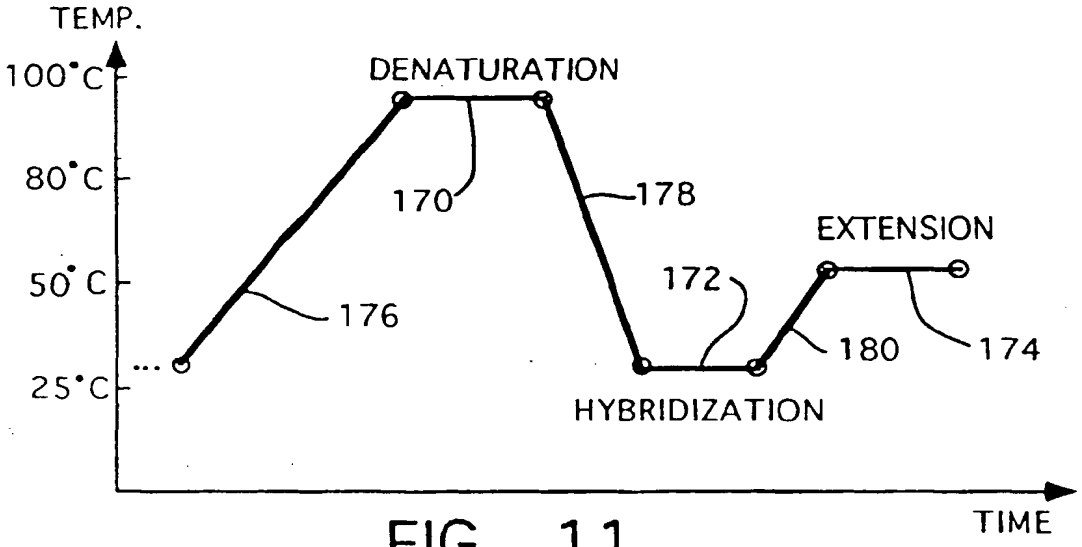

FIG. 11

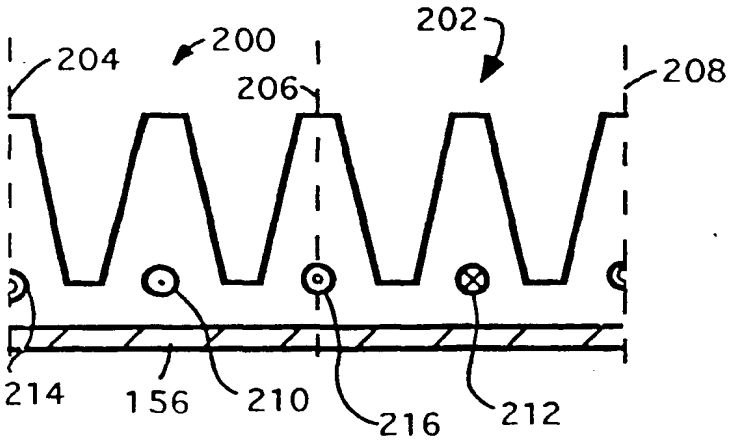

FIG. 12

BNSDOCID: <EP___0810030A1_I_>

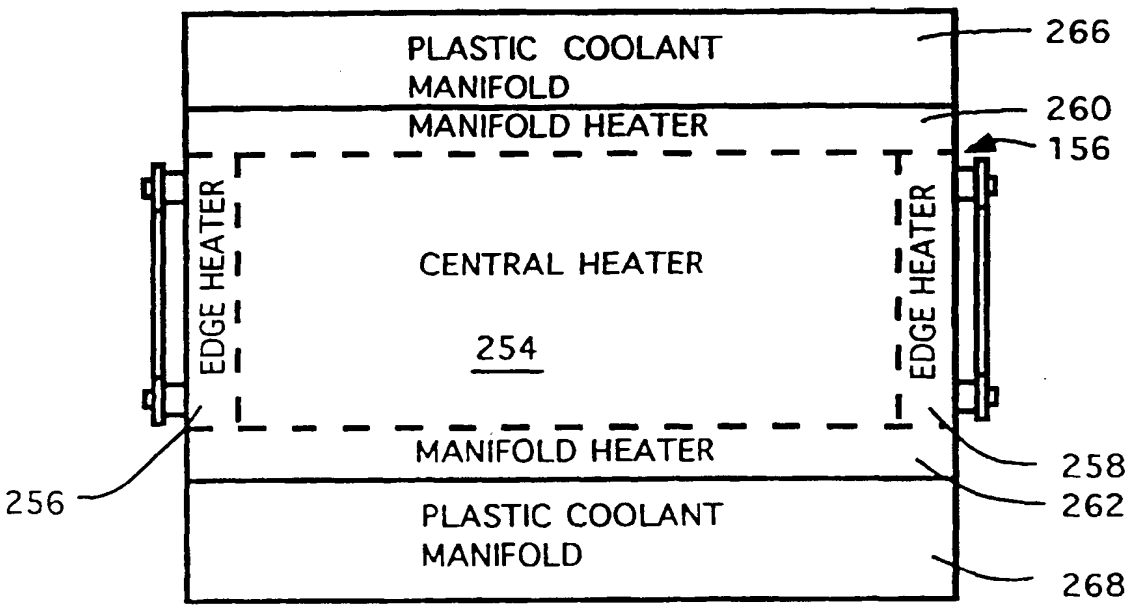

FIG. 13

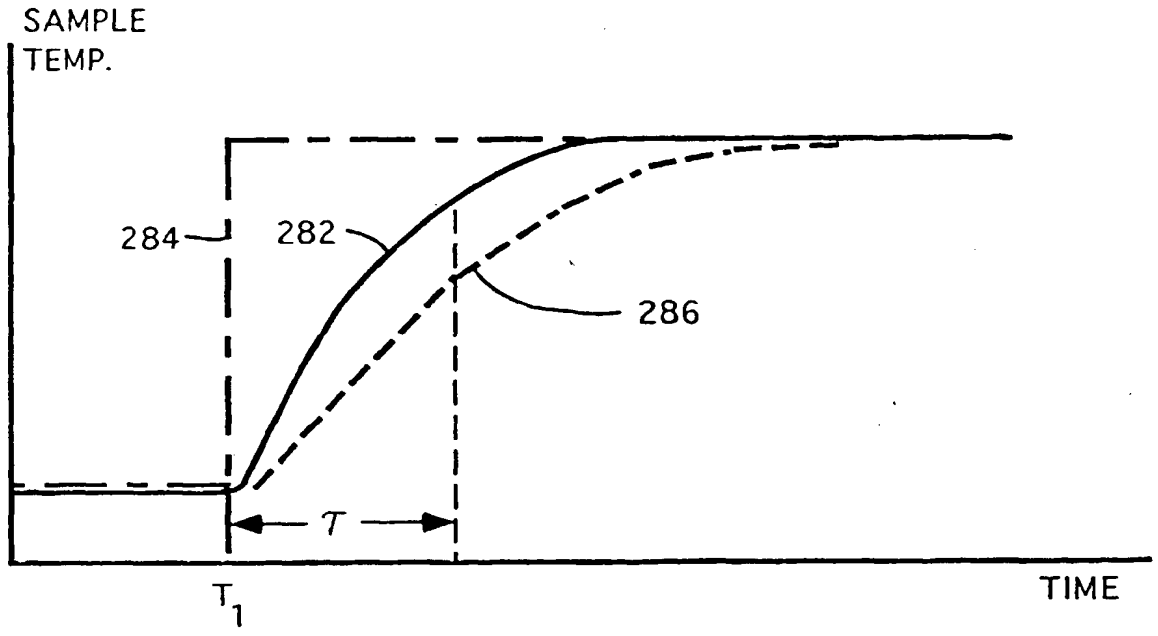

FIG. 14

BNSDOCID: <EP___0810030A1_I_>

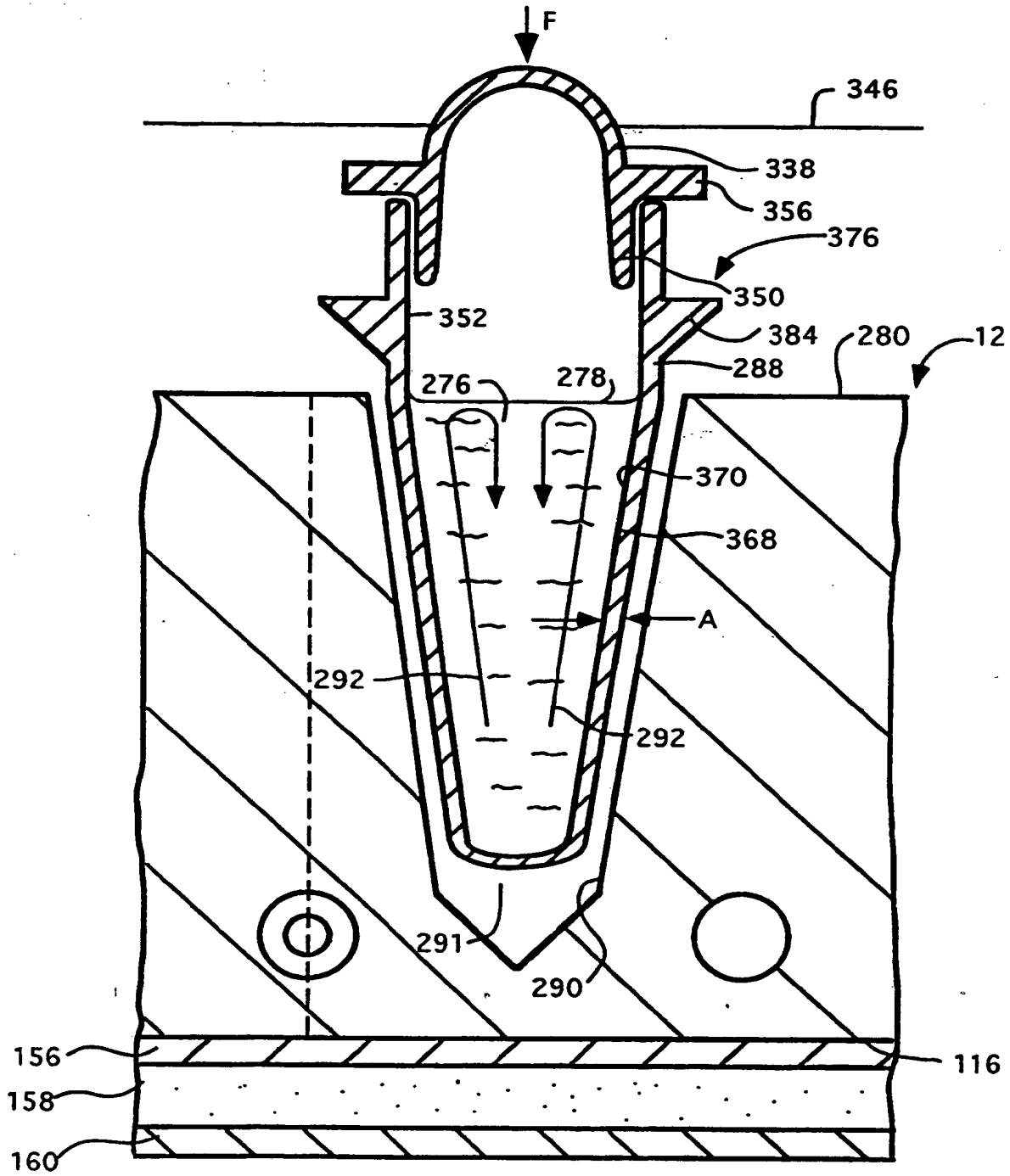

FIG. 15

BNSDOCID: <EP___0810030A1_I_>

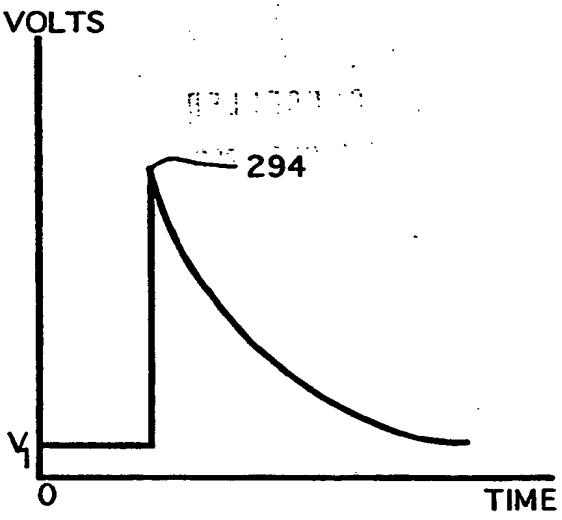

FIG. 16A

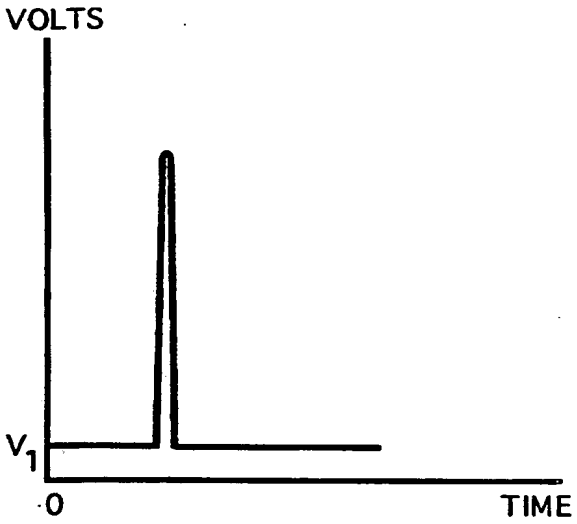

FIG. 16B

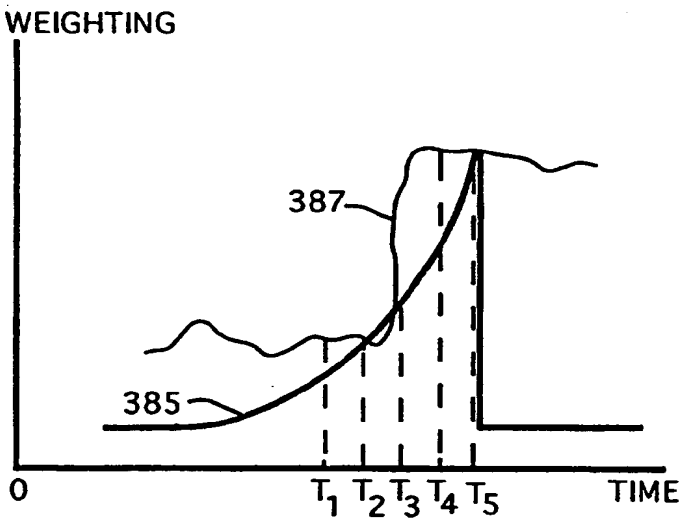

FIG. 16C

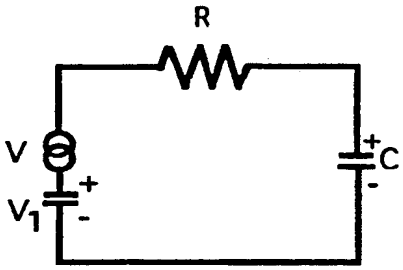

FIG. 16D

BNSDOCID: <EP___0810030A1_I_>

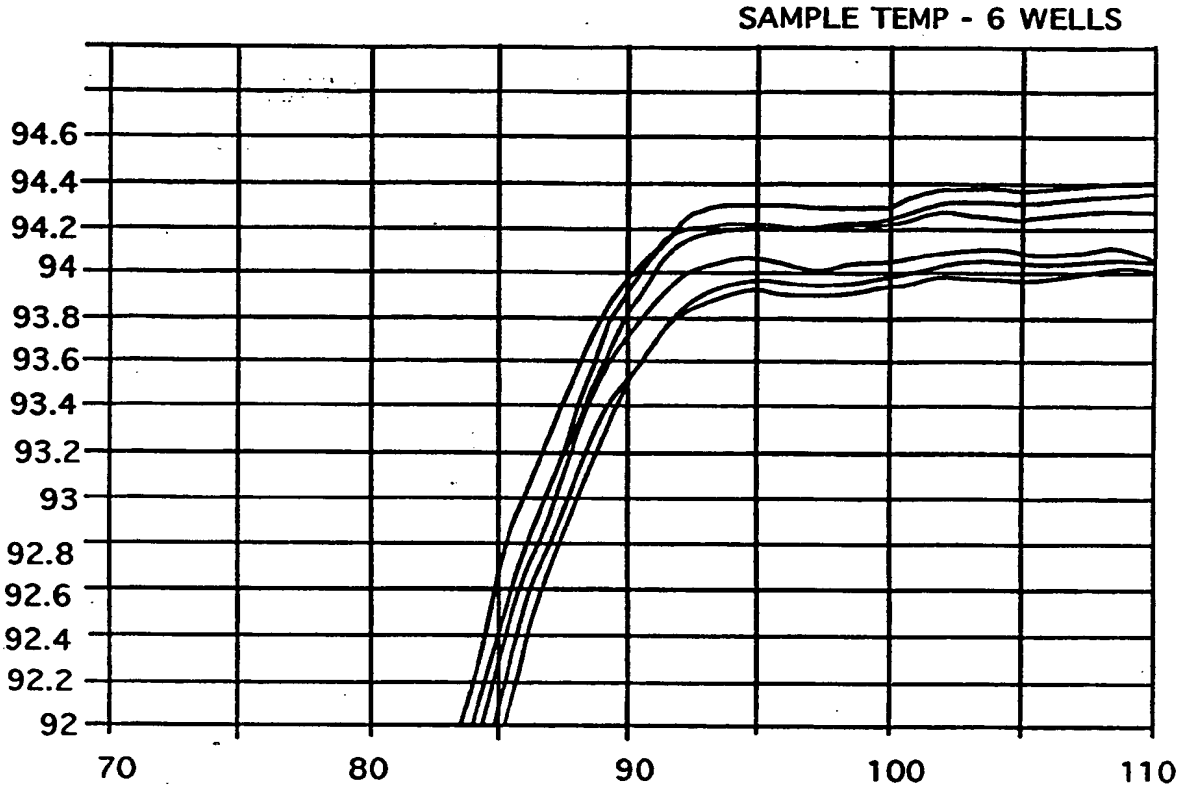

FIG. 17

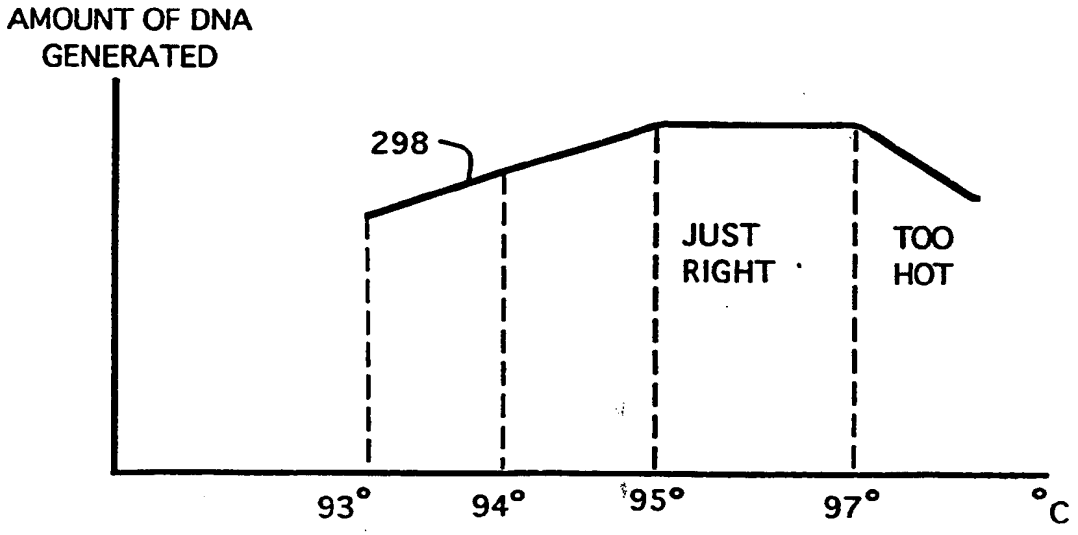

FIG. 18

BNSDOCID: <EP___0810030A1_I_>

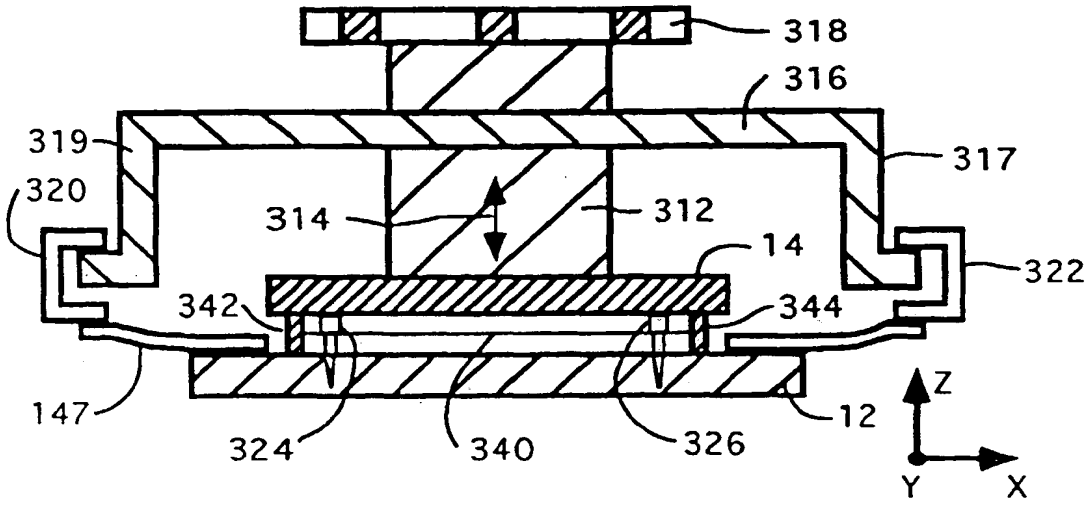

FIG. 19

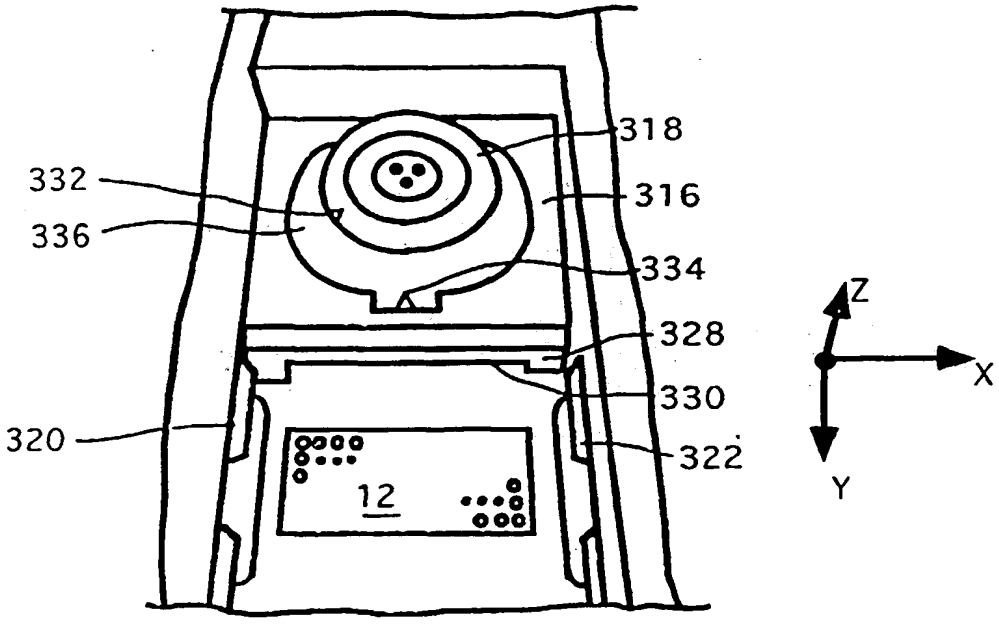

FIG. 20

BNSDOCID: <EP___0810030A1_I_>

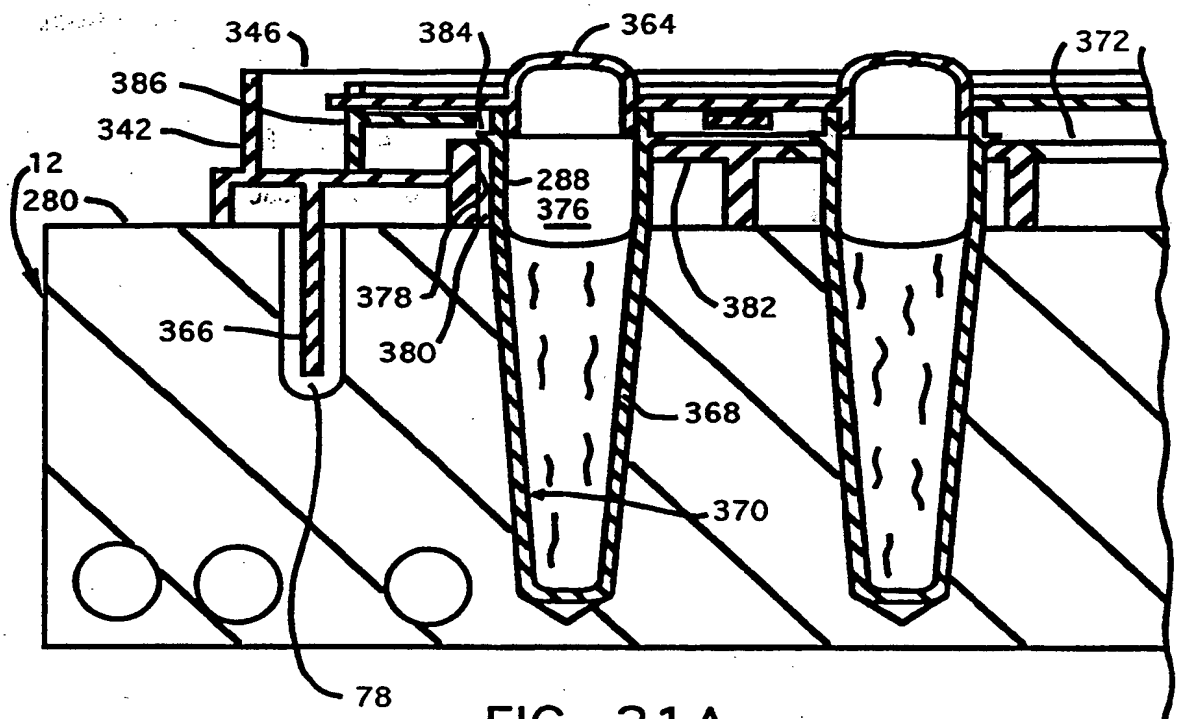

FIG 21A

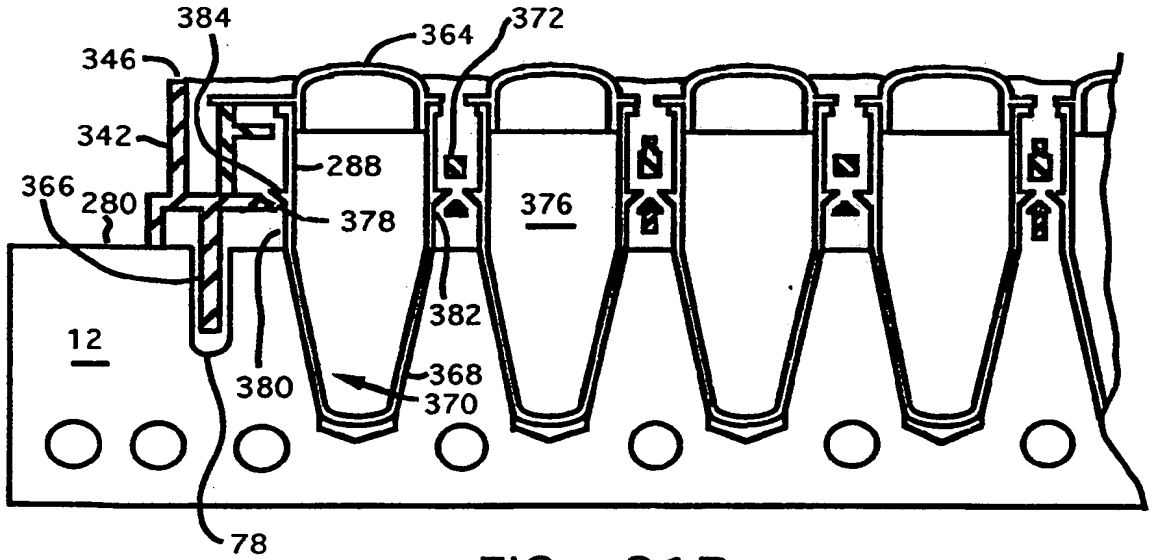

FIG. 21B

BNSDOCID: <EP___0810030A1_I_>

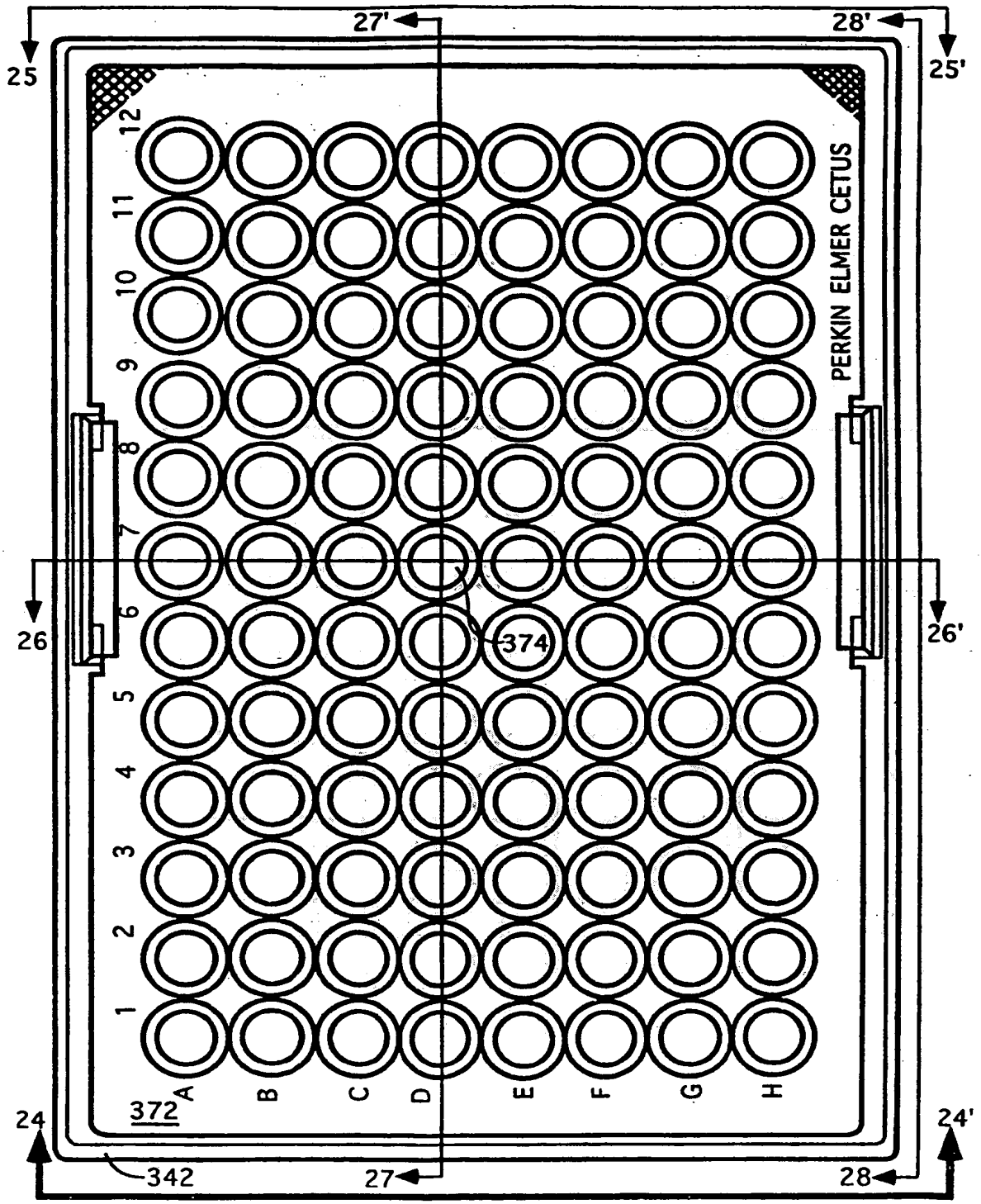

FIG. 22

BNSDOCID: <EP___0810030A1_I_>

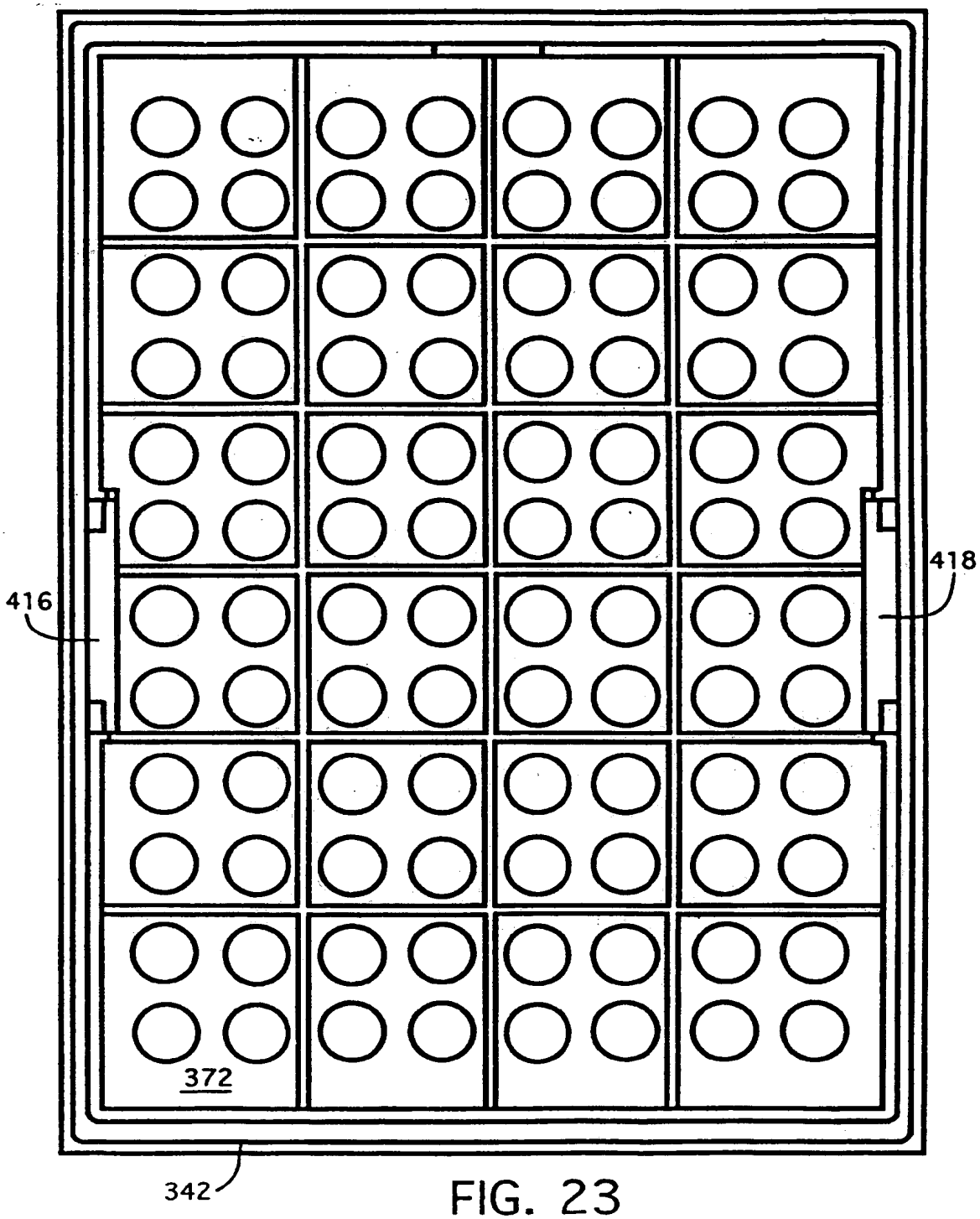

FIG. 23

BNSDOCID: <EP___0810030A1_I_>

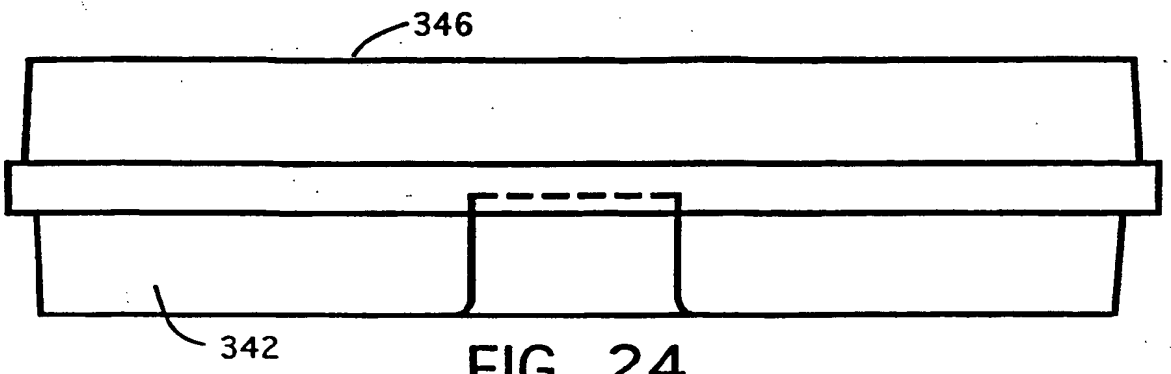

FIG. 24

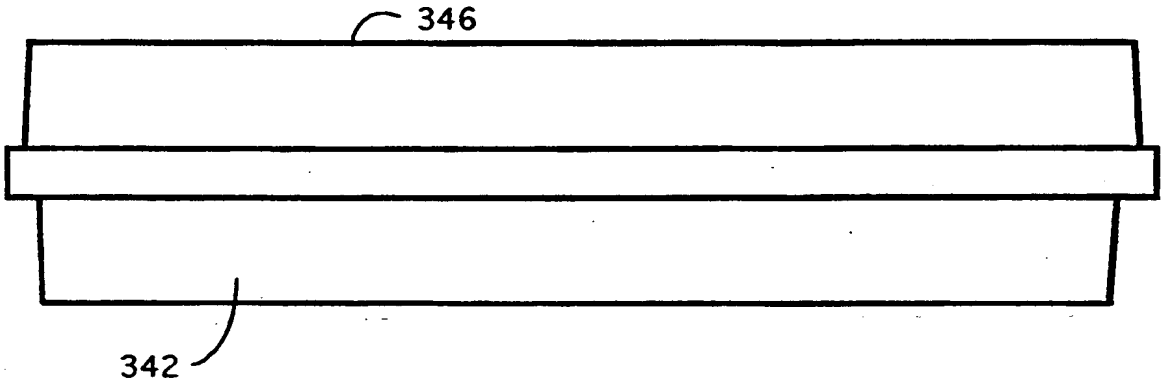

FIG. 25

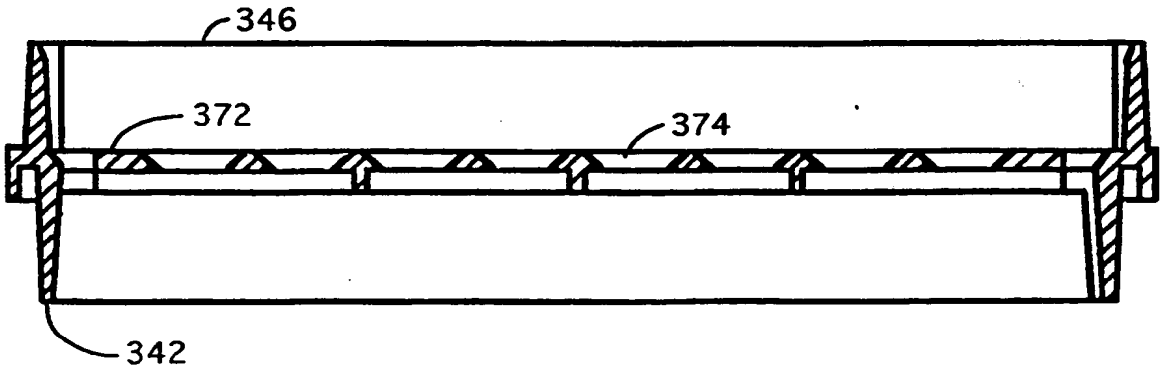

FIG. 26

BNSDOCID: <EP___0810030A1_I_>

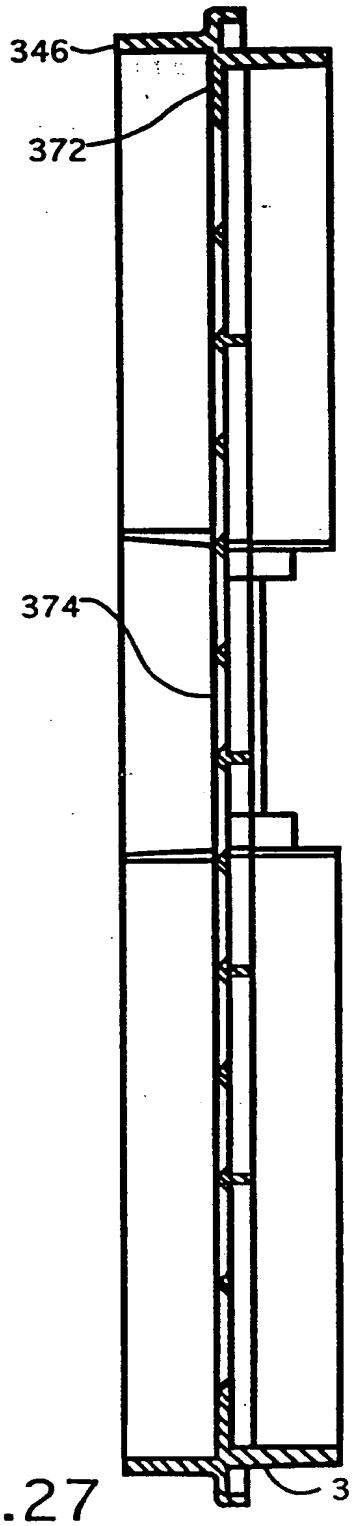

FIG.27

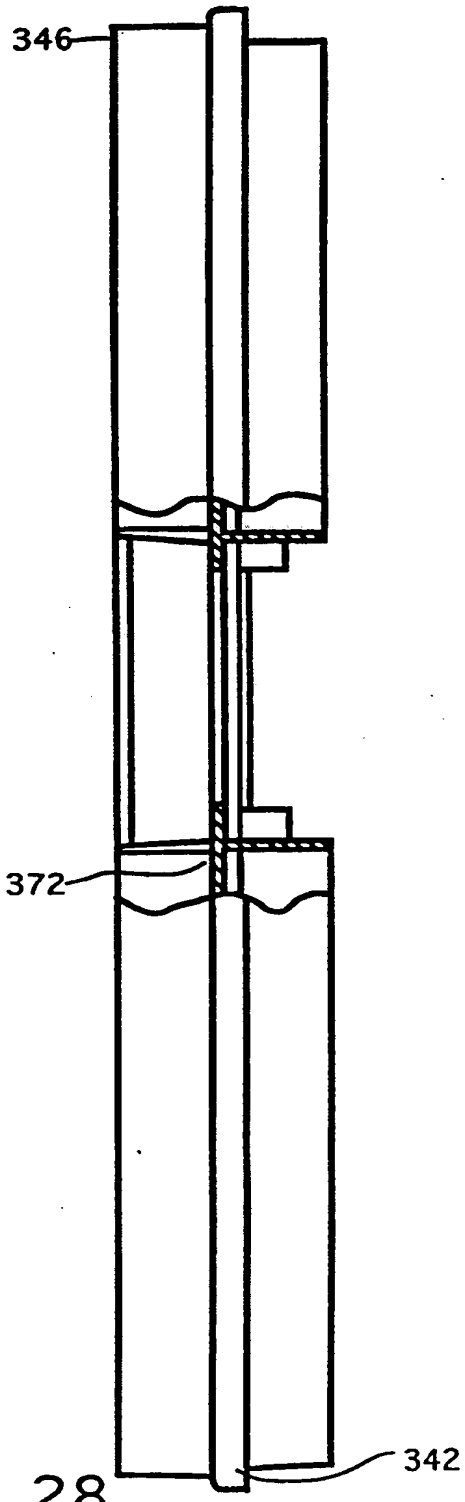

FIG. 28

BNSDOCID: <EP___0810030A1_I_>

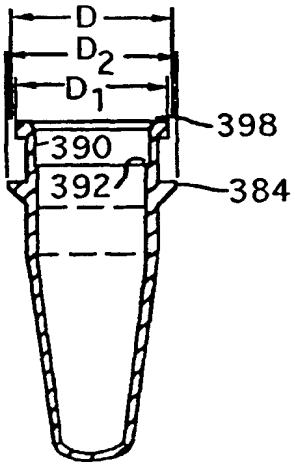

FIG 29

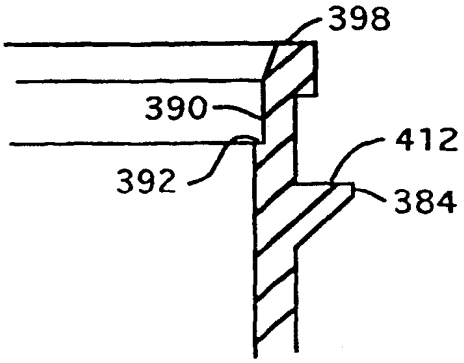

FIG 30

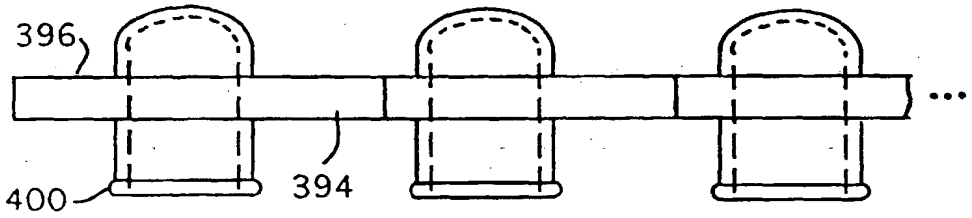

FIG 31

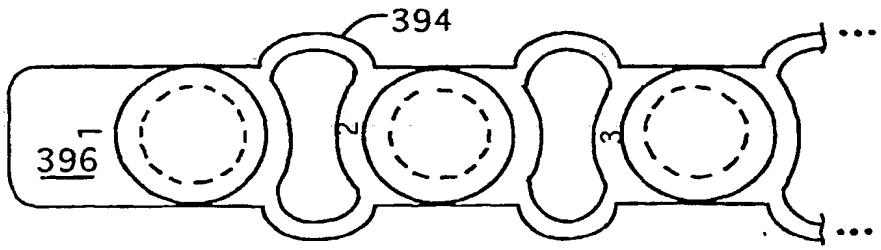

FIG 32

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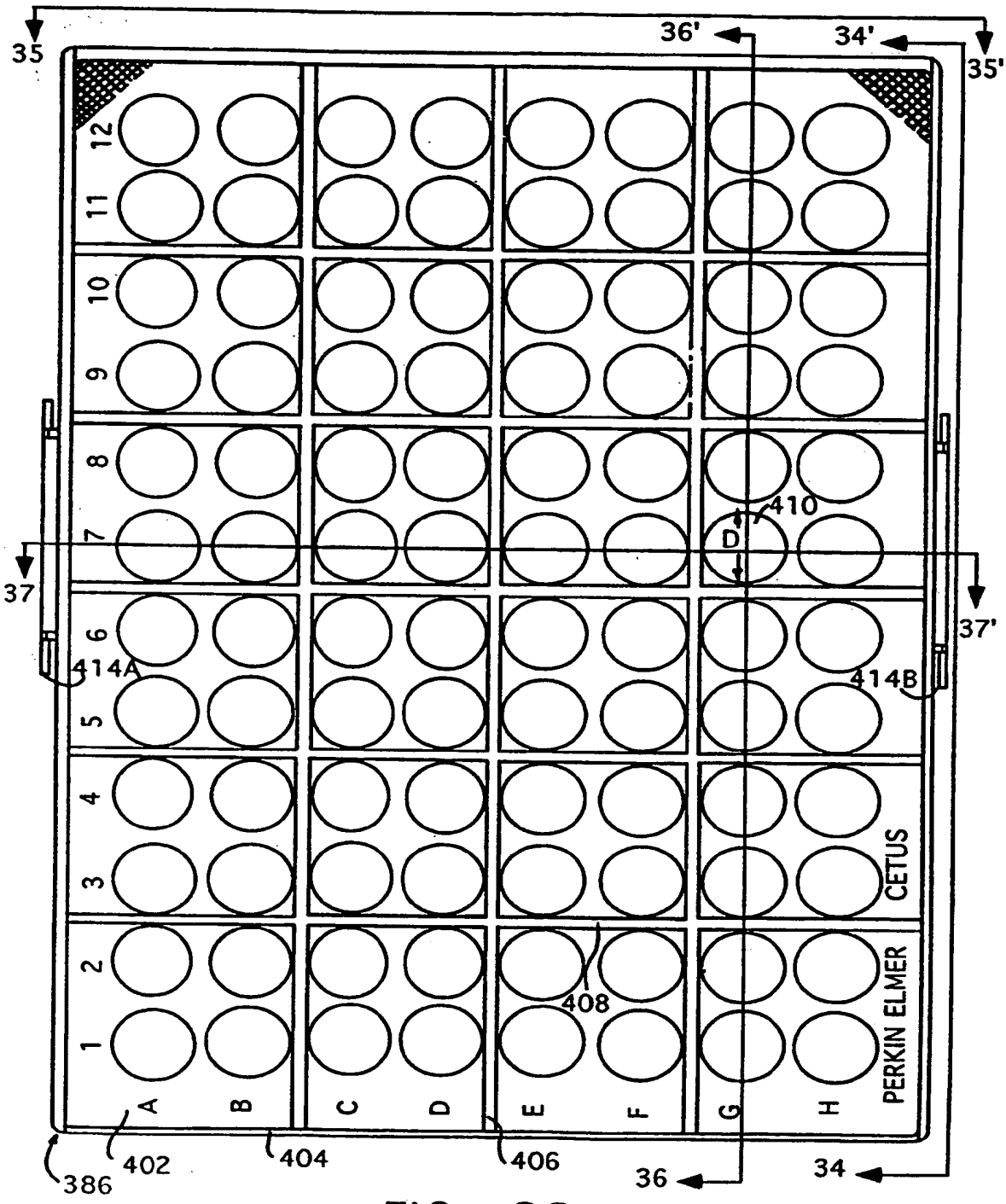

FIG. 33

BNSDOCID: <EP___0810030A1_I_>

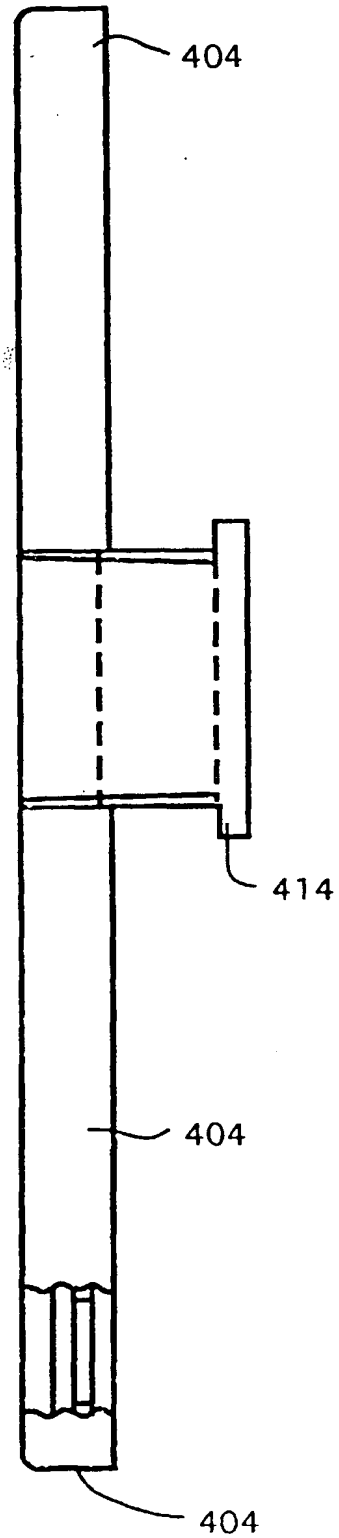

FIG. 34

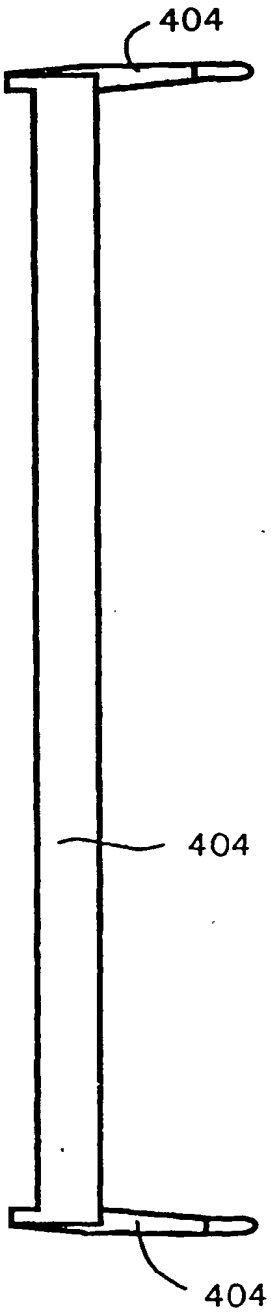

FIG.35

BNSDOCID: <EP___0810030A1_I_>

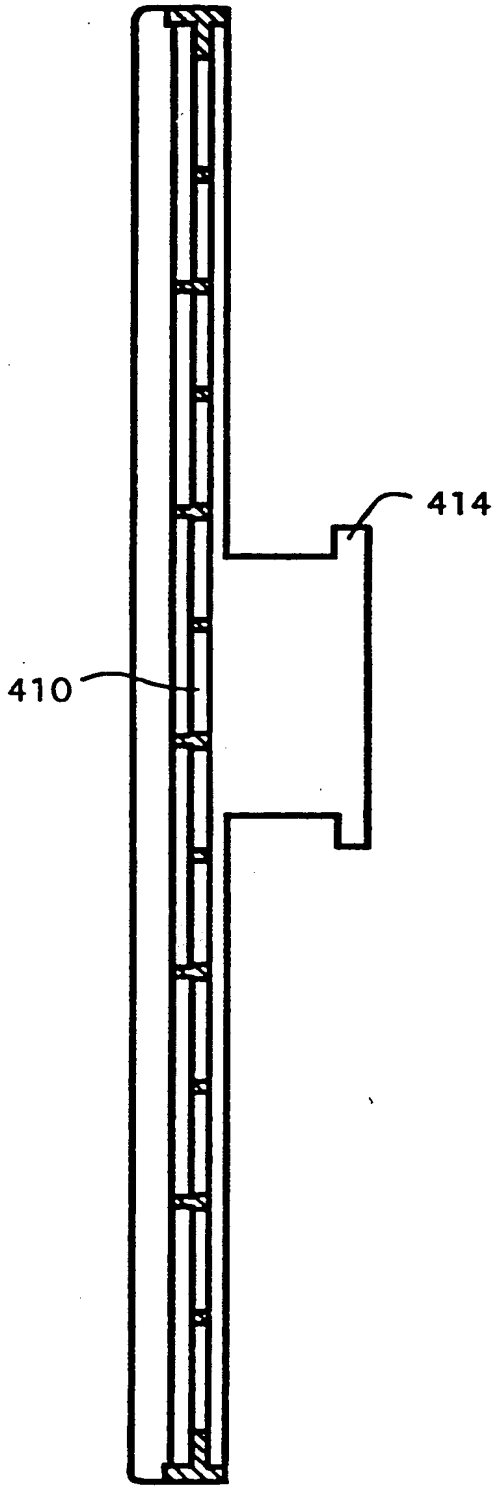

FIG. 36

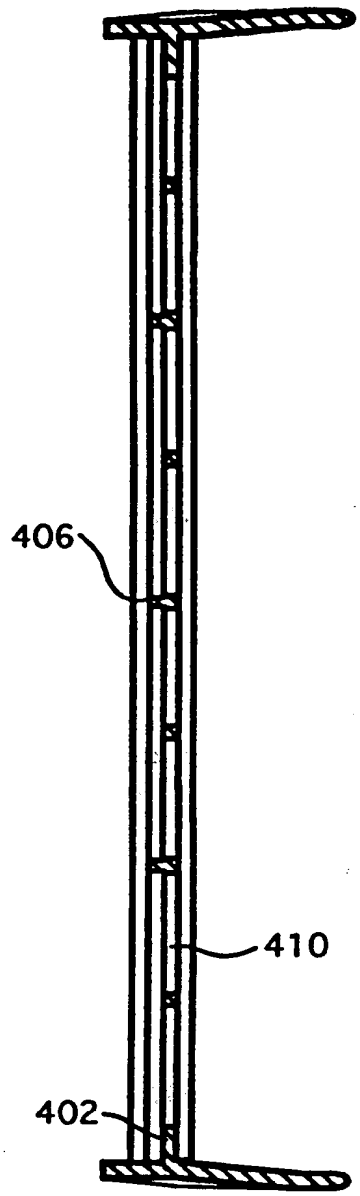

FIG. 37

BNSDOCID: <EP___0810030A1_I_>

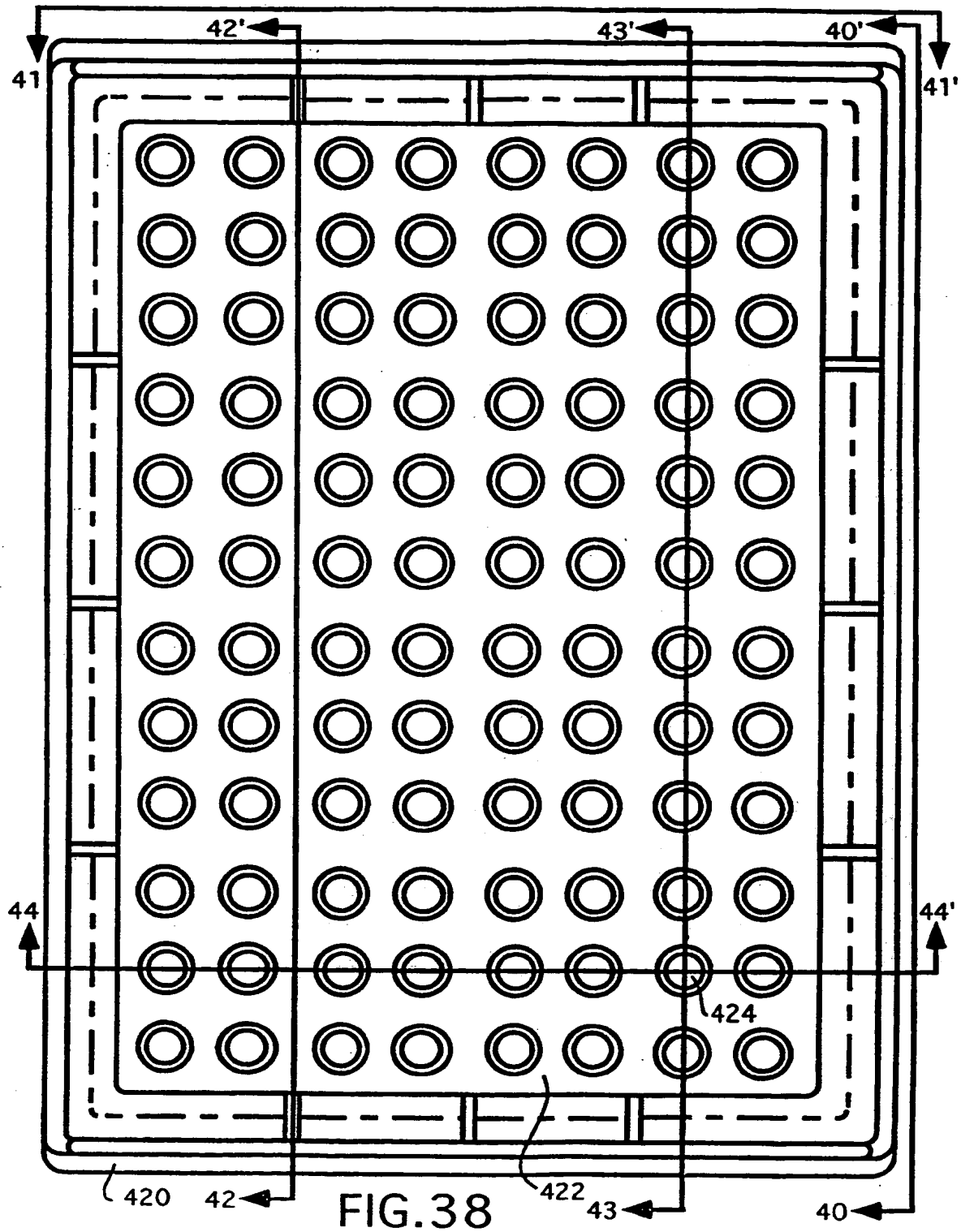

FIG.38

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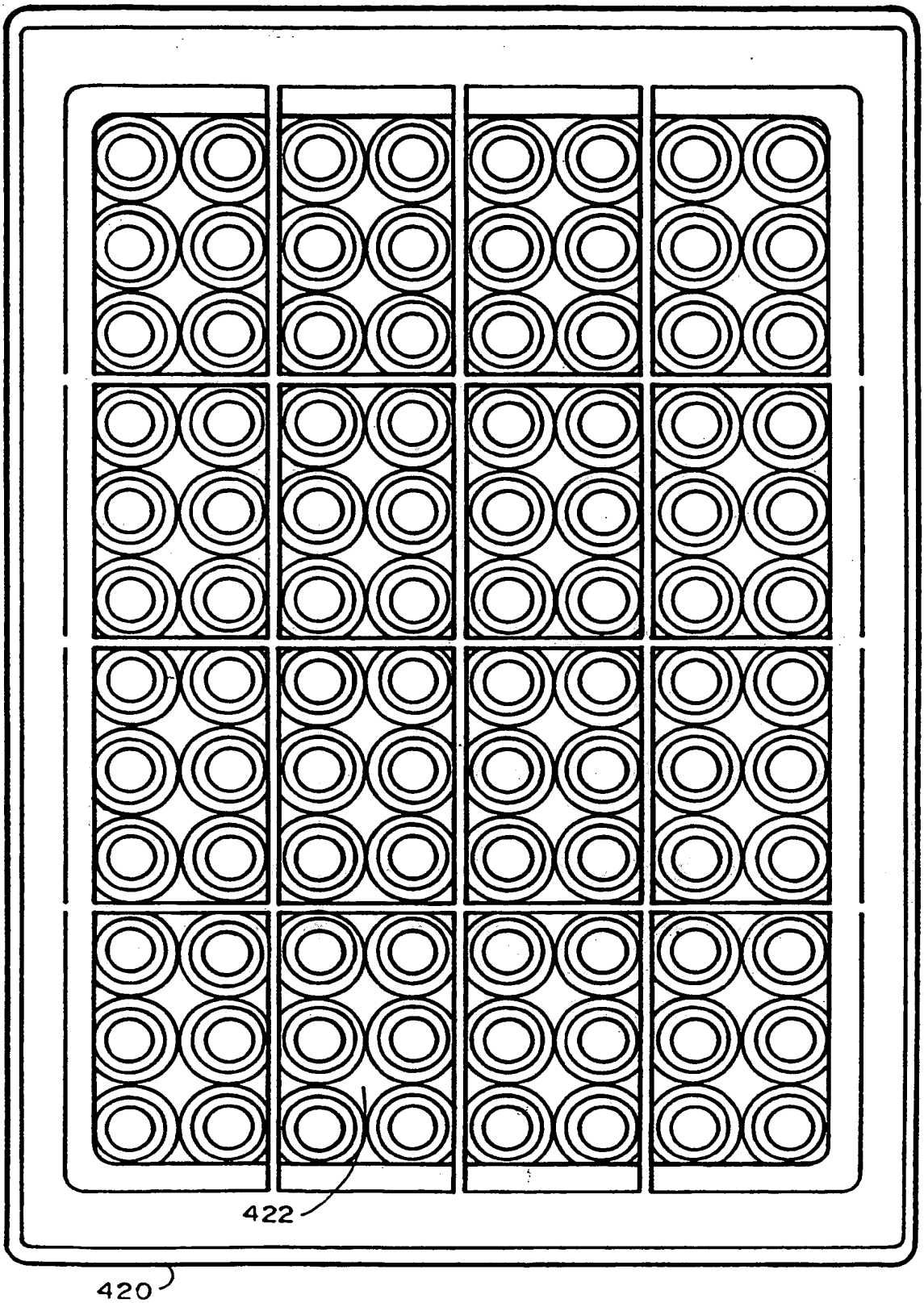

FIG. 39

BNSDOCID: <EP___0810030A1_I_>

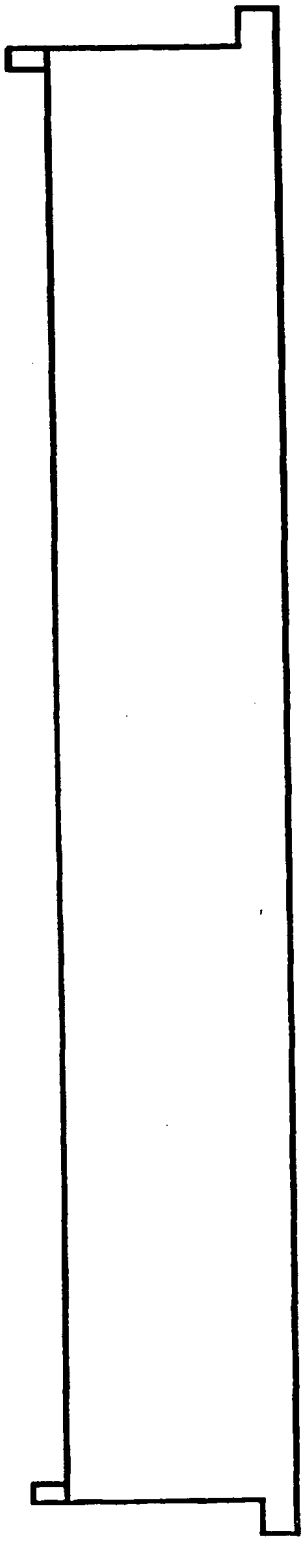

FIG. 40

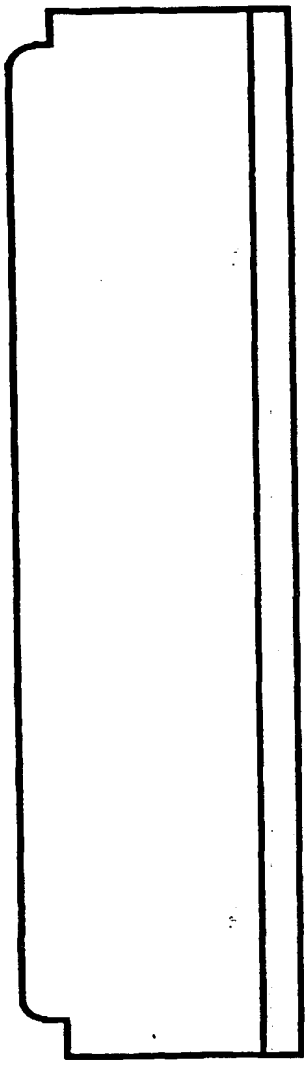

FIG. 41

BNSDOCID: <EP___0810030A1_I_>

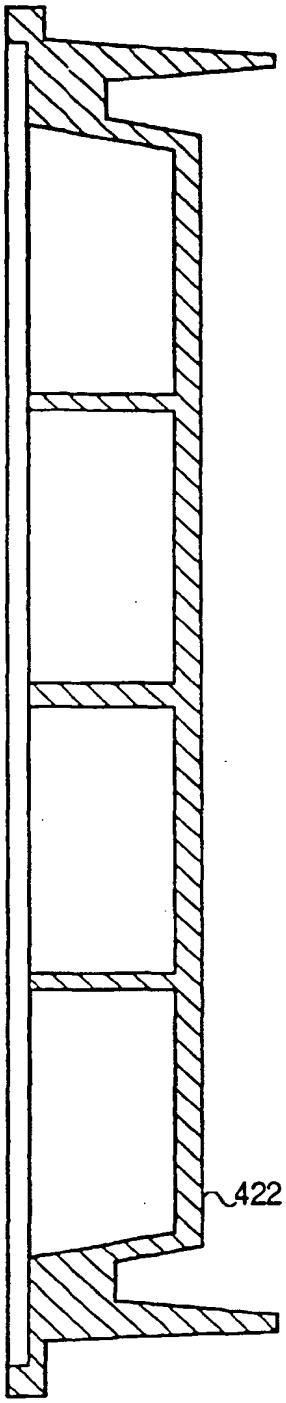

FIG. 42

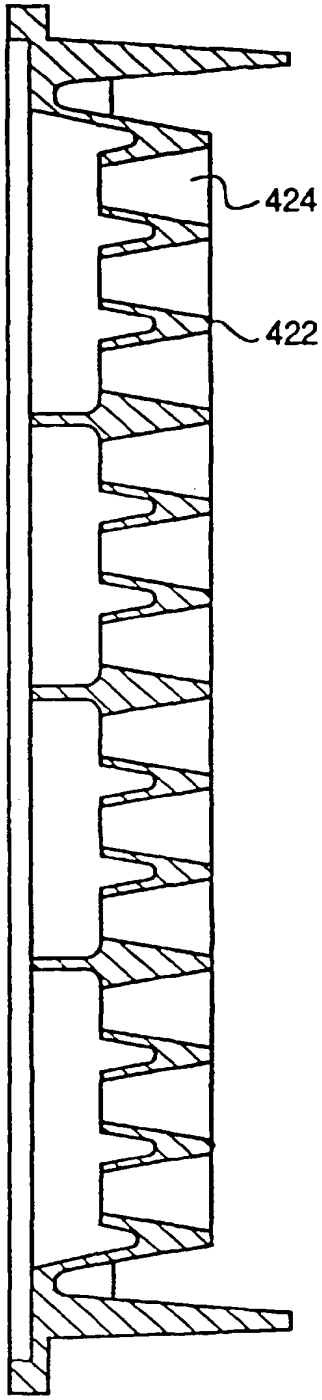

FIG. 43

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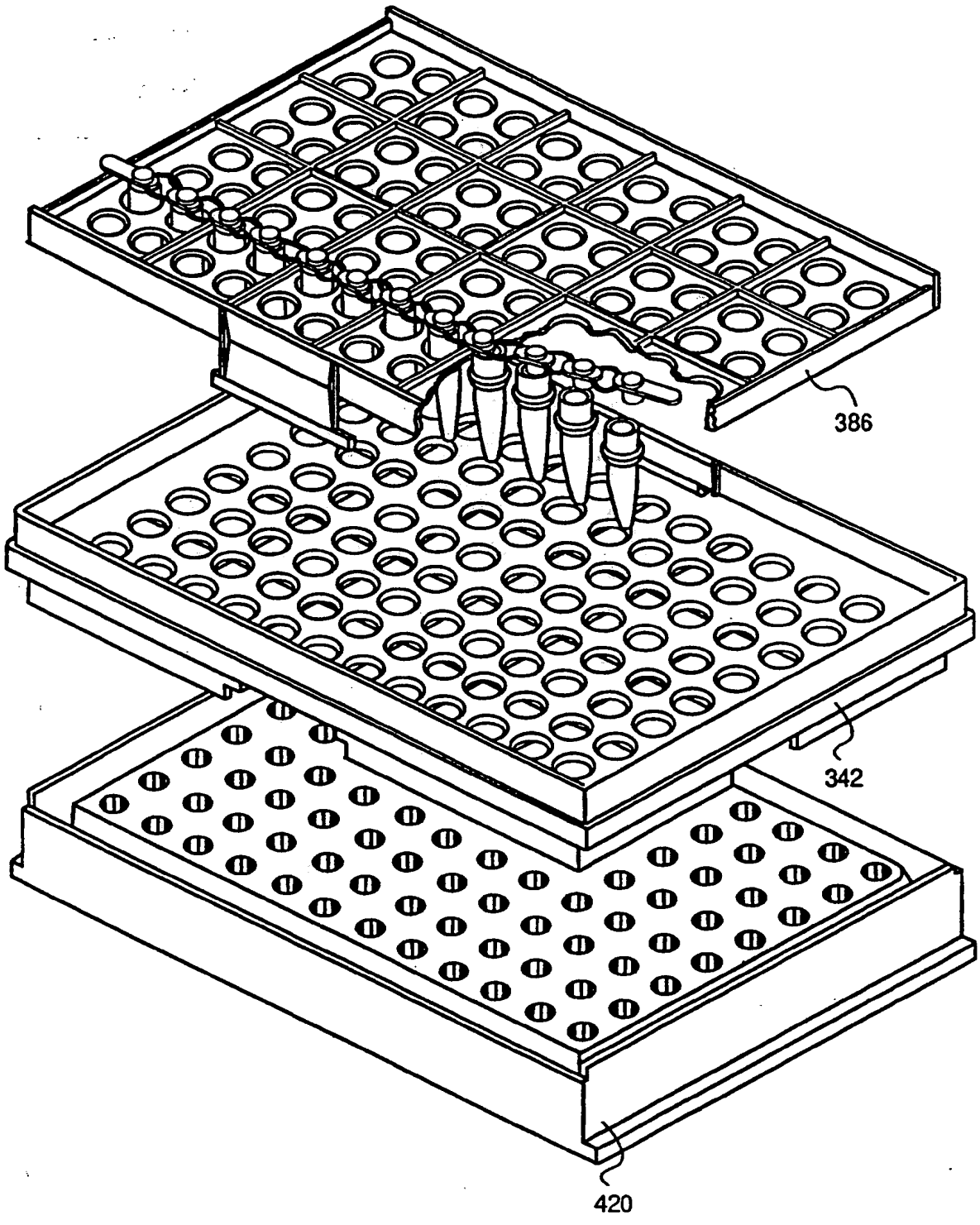

FIG. 45

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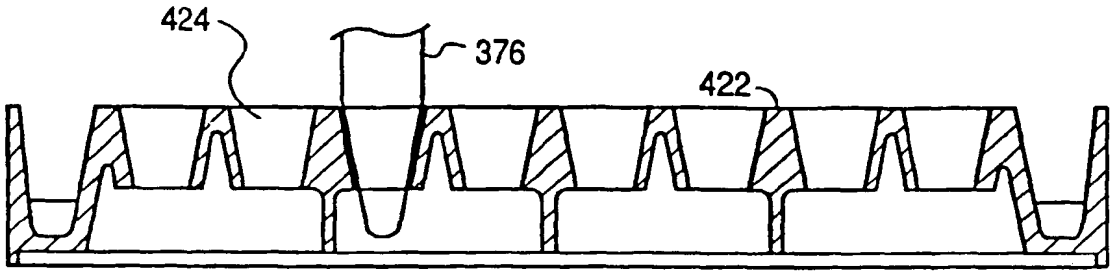


FIG. 44

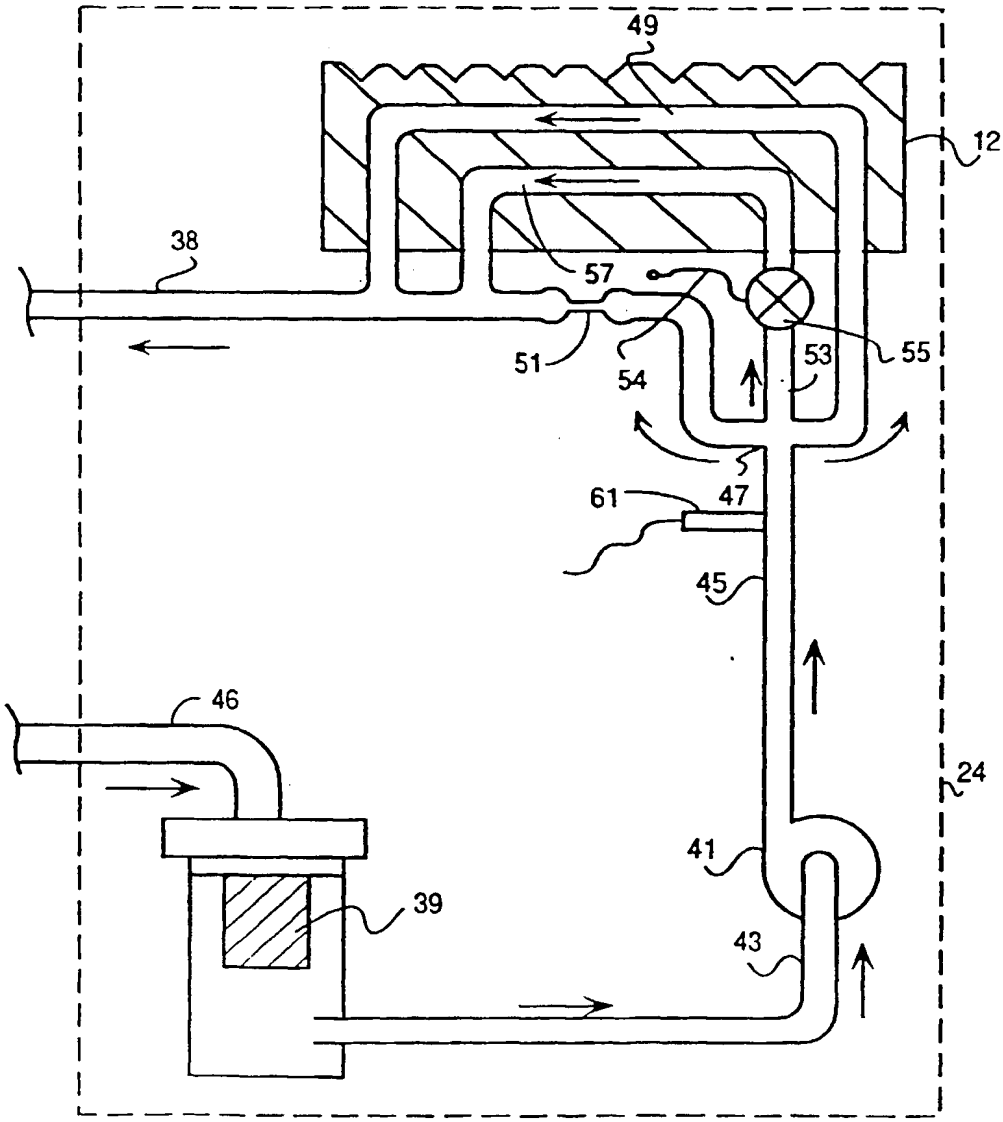
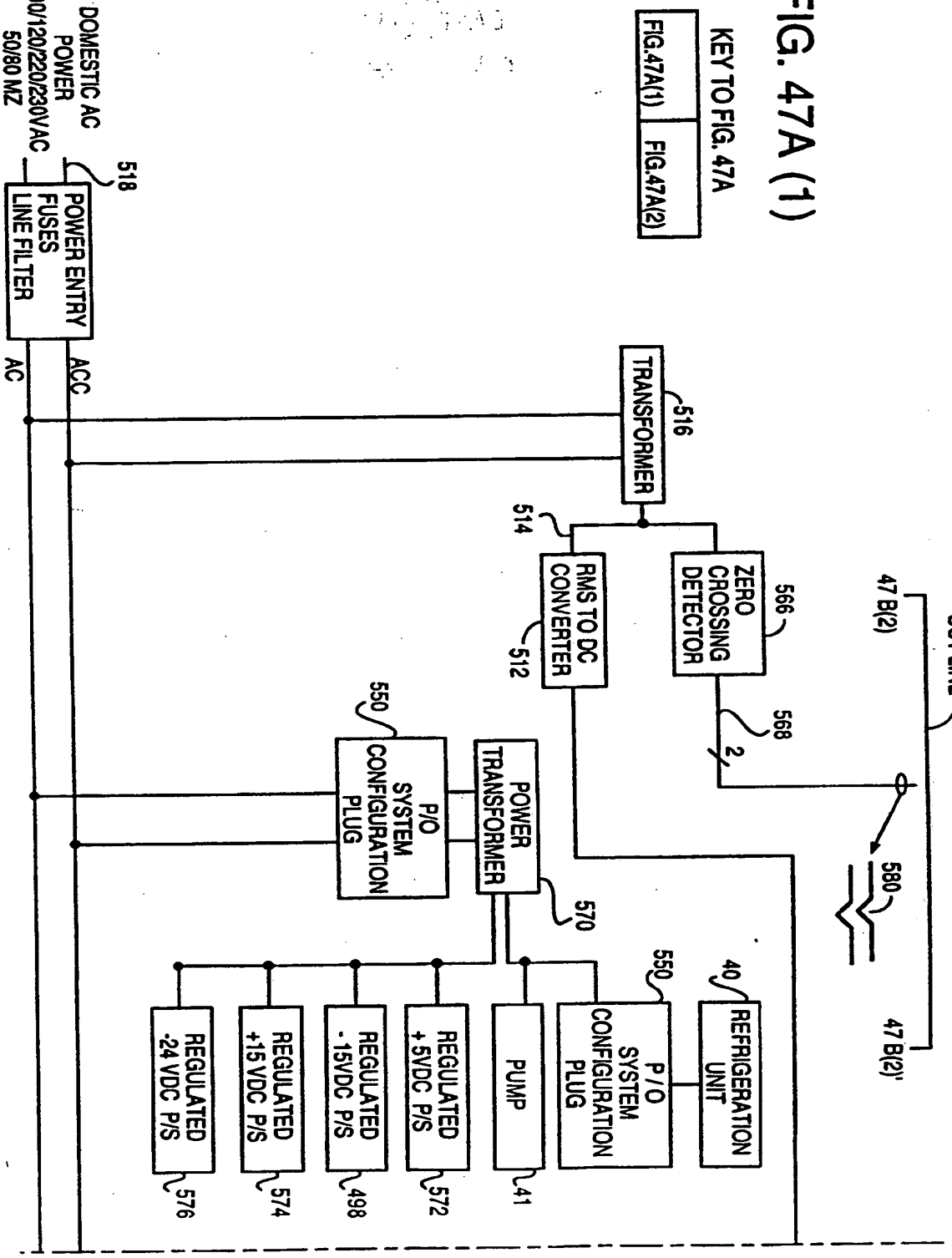


FIG. 46

BNSDOCID: <EP___0810030A1_I_>

FIG. 47A (1)



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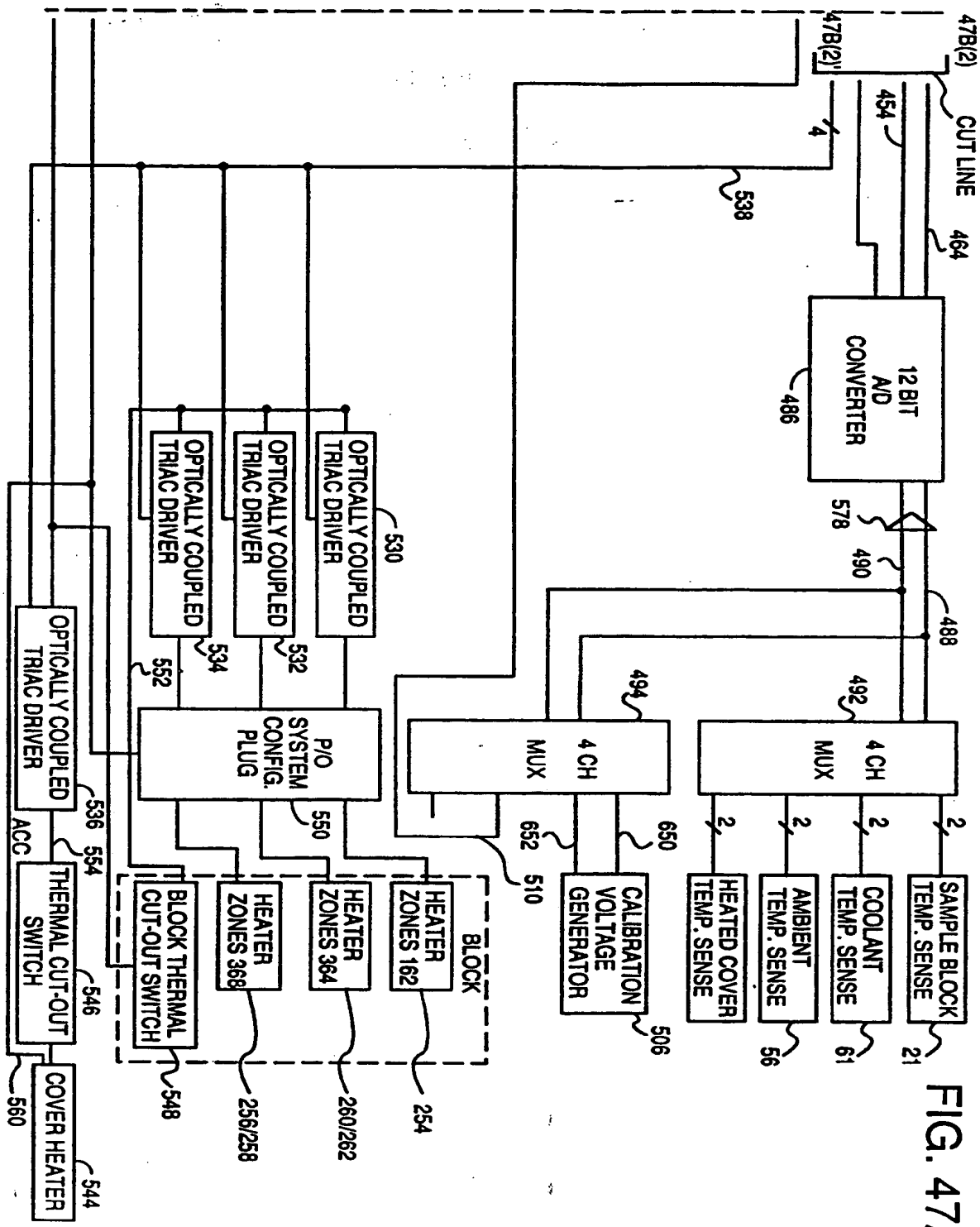

FIG. 47A (2)

BNSDOCID: <EP___0810030A1_I_>

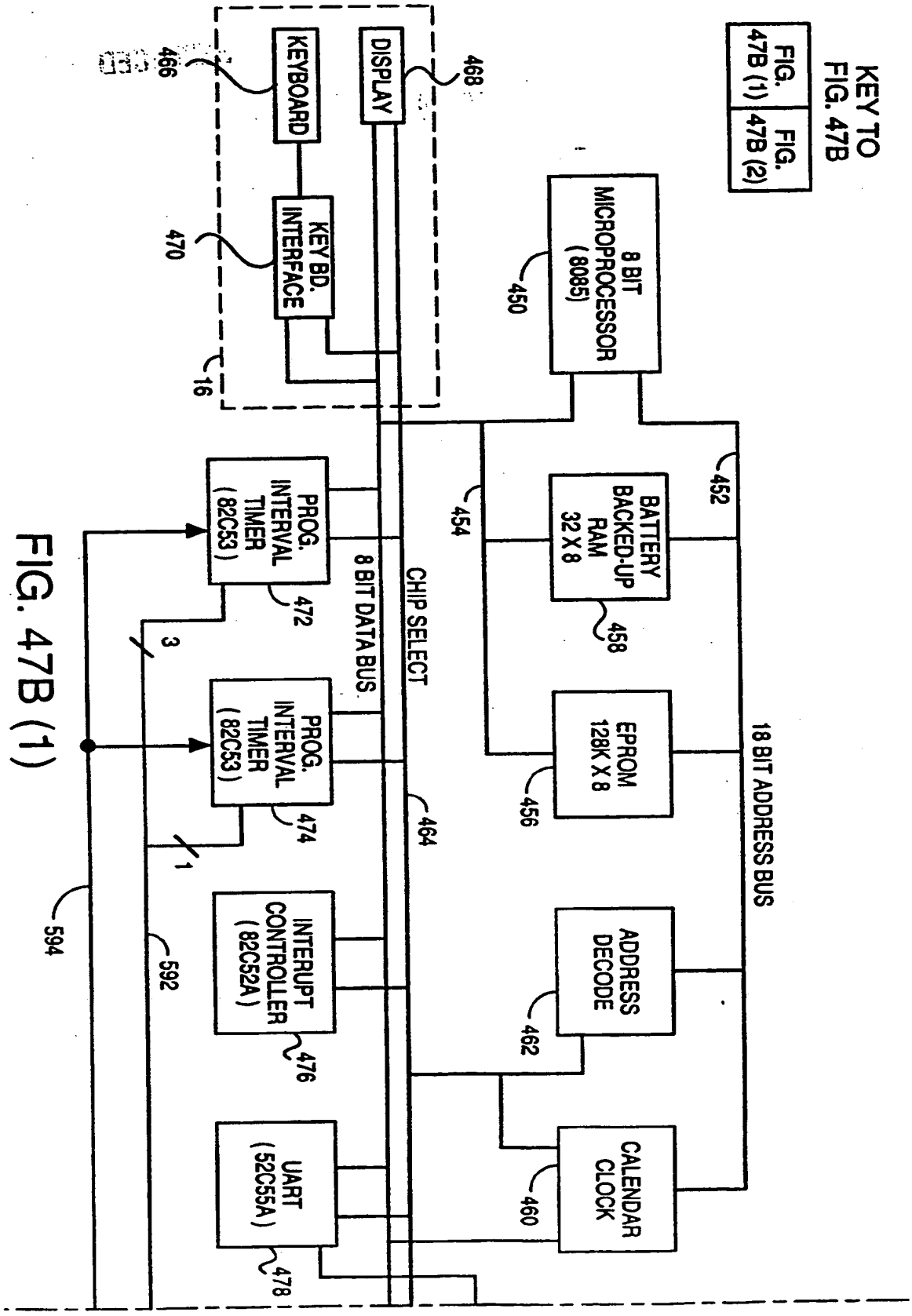

FIG. 47B (1)

BNSDOCID: <EP___0810030A1_I_>

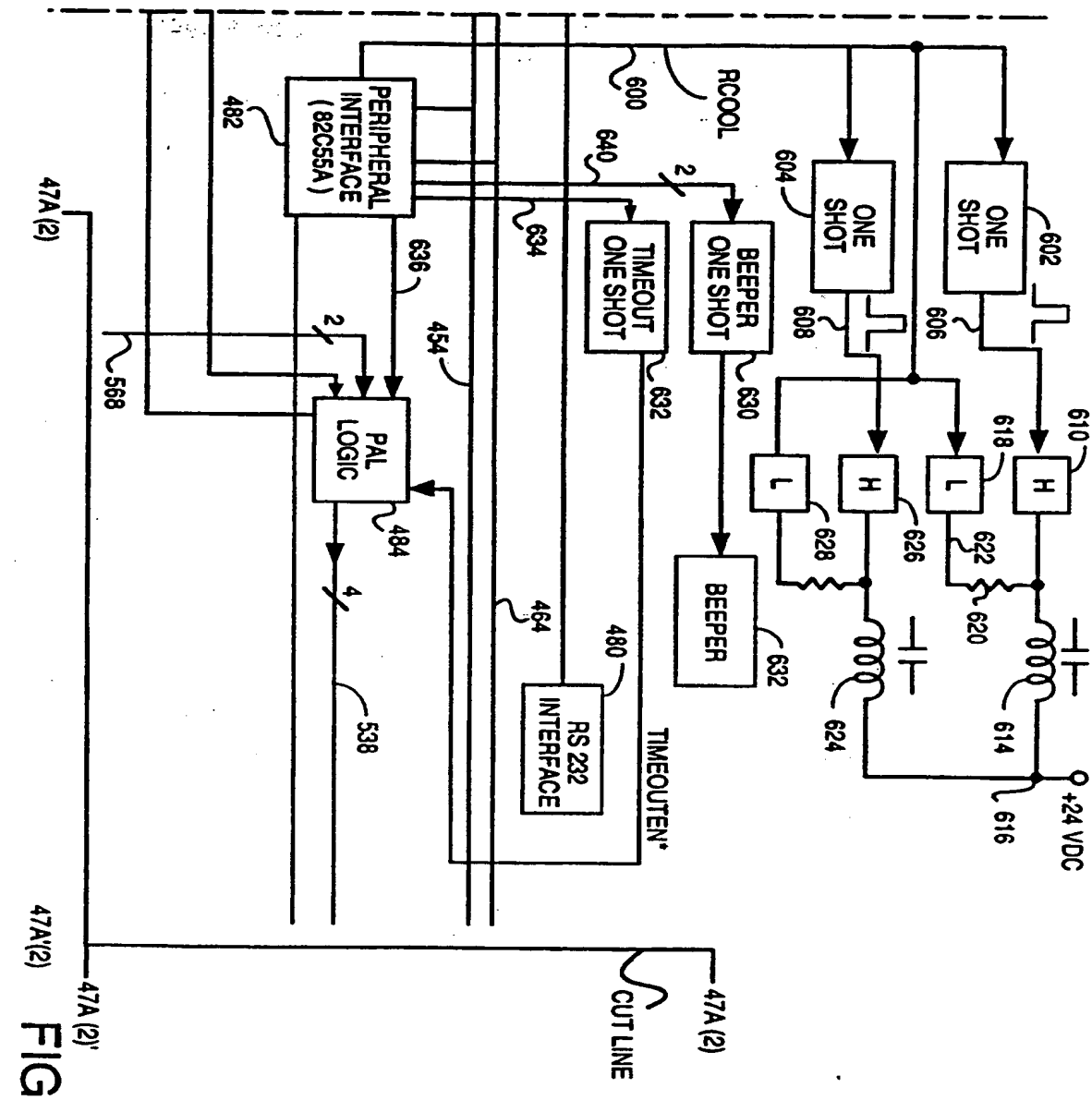

FIG. 47B (2)

BNSDOCID: <EP___0810030A1_I_>

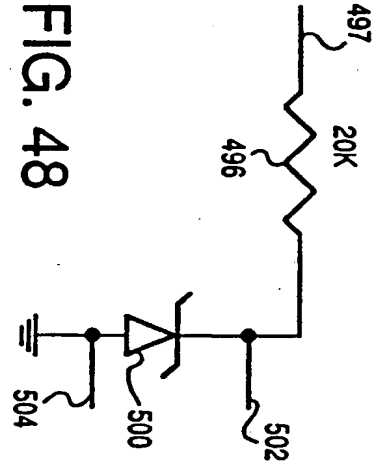

FIG. 48

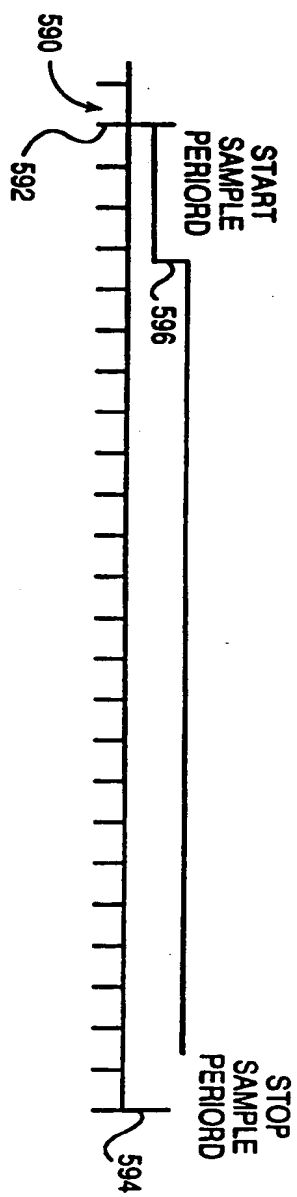

FIG. 49

BNSDOCID: <EP___0810030A1_I_>

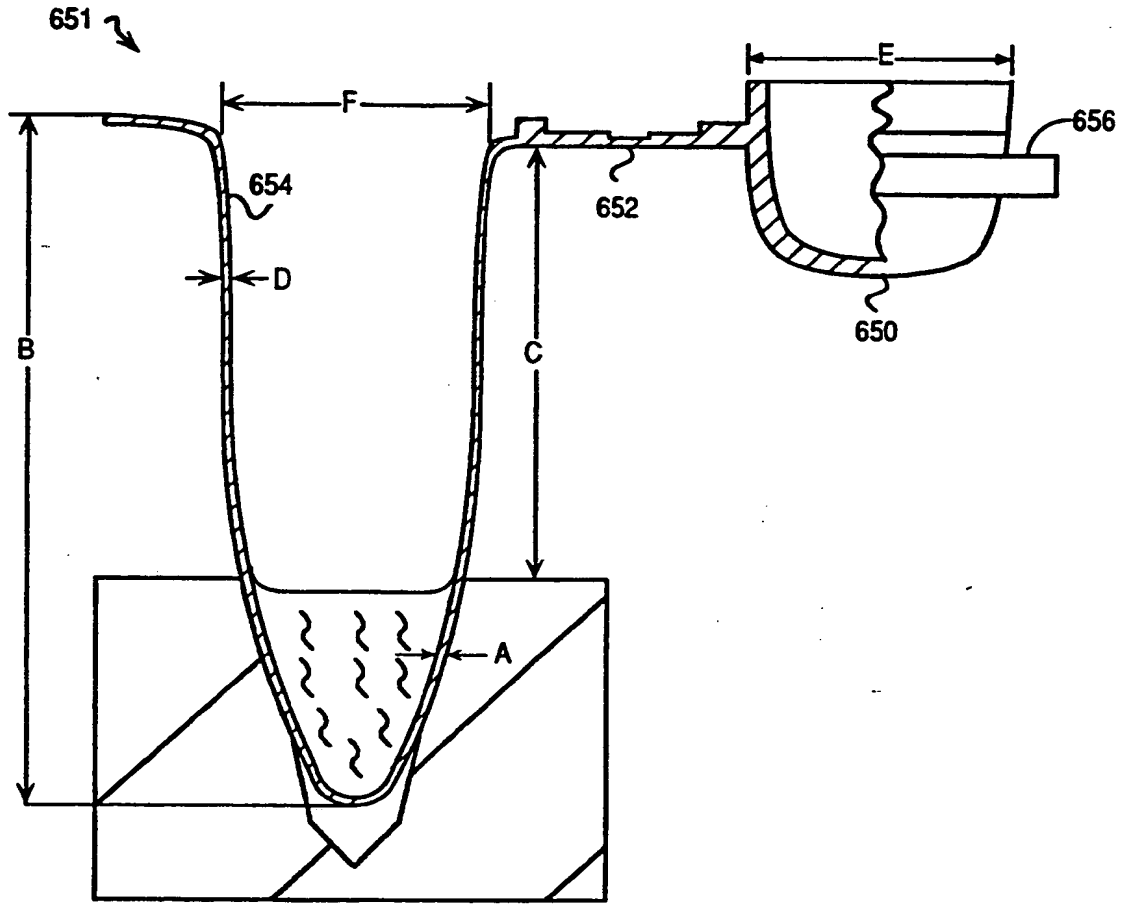

FIG. 50

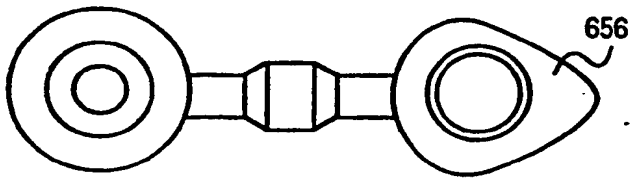

FIG. 52

BNSDOCID: <EP___0810030A1_I_>

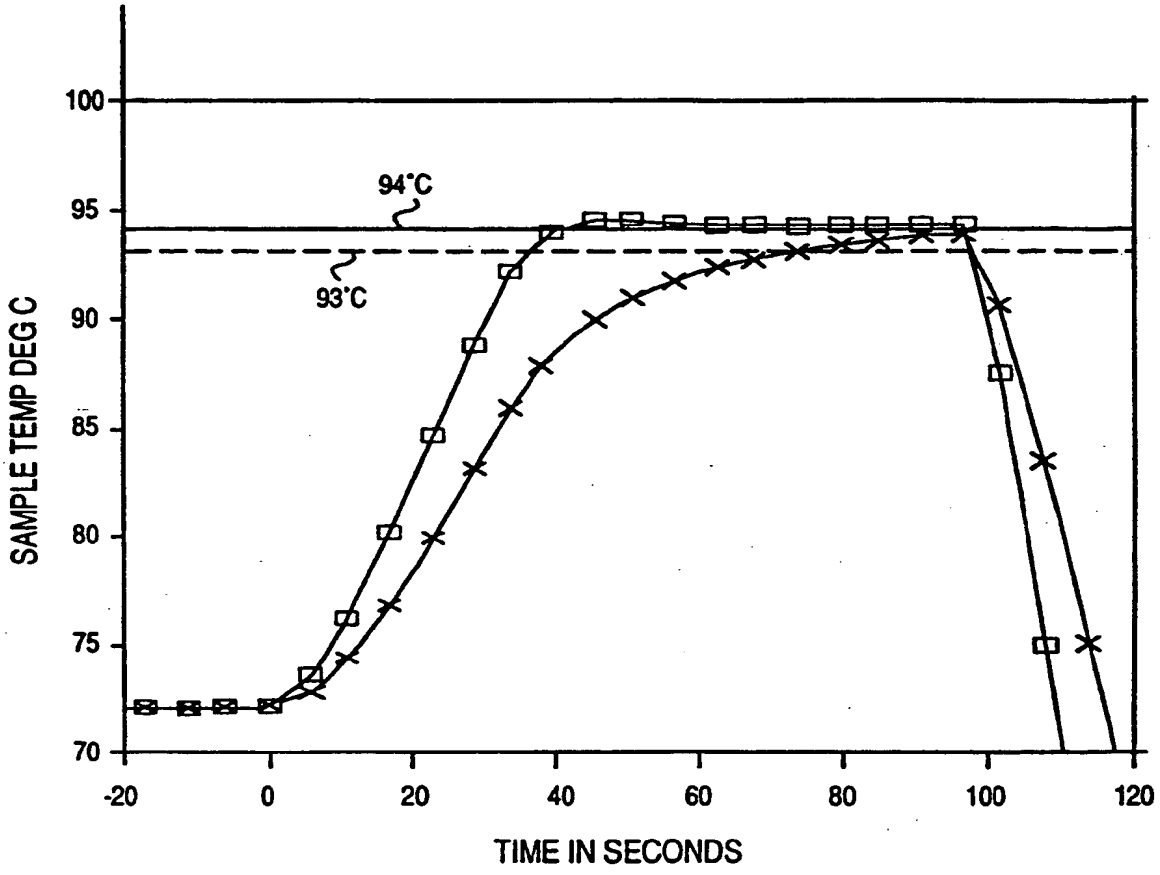

FIG. 51

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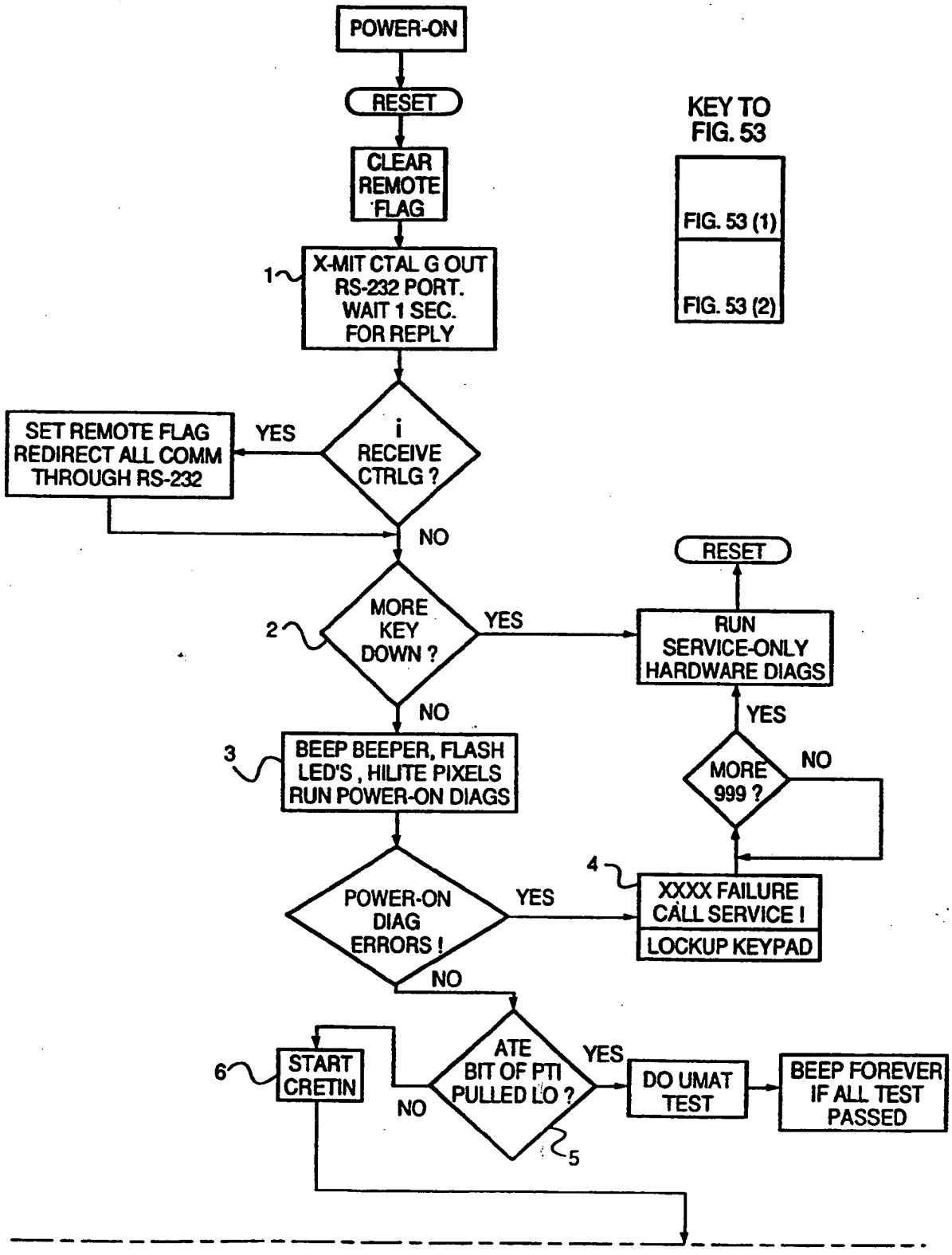

FIG. 53 (1)

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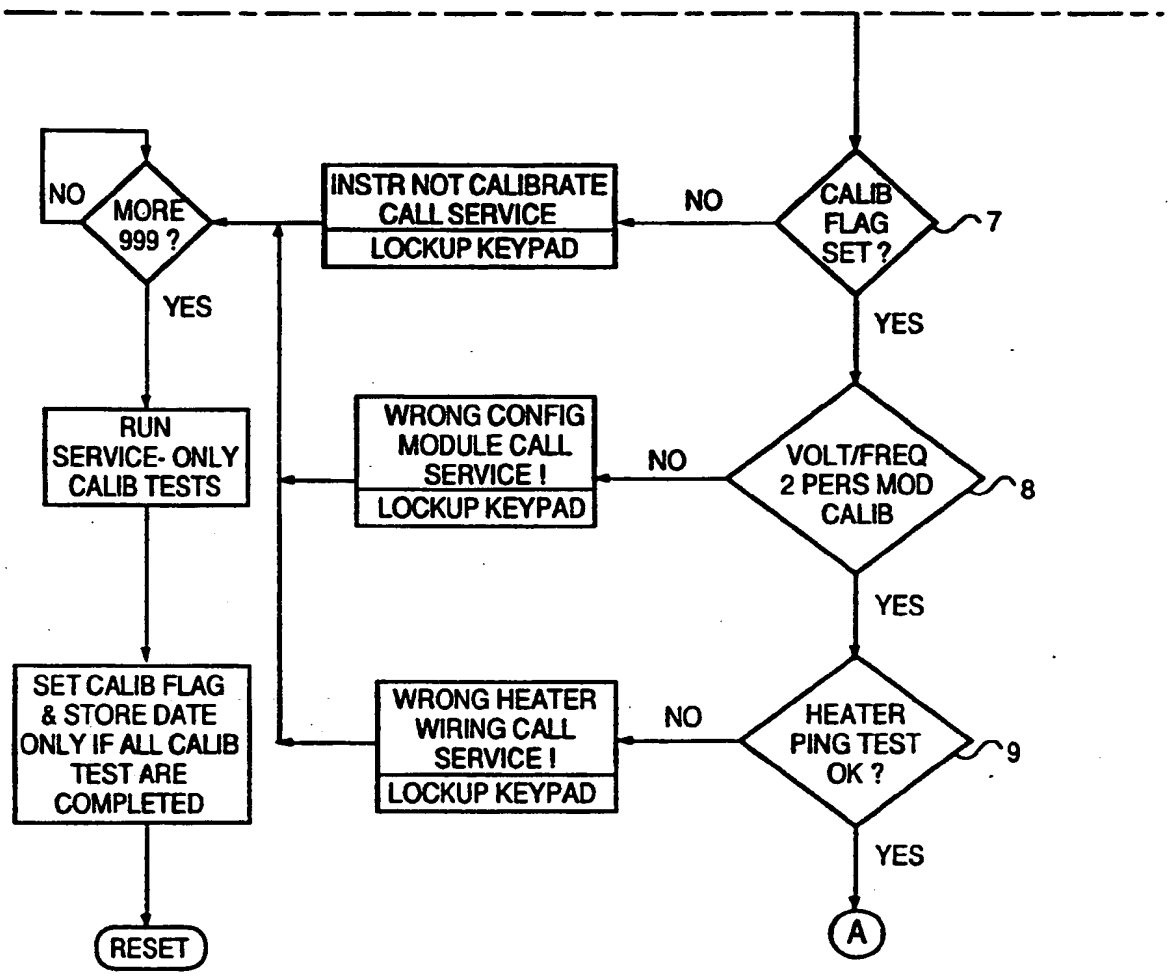

FIG. 53 (2)

BNSDOCID: <EP___0810030A1_I_>

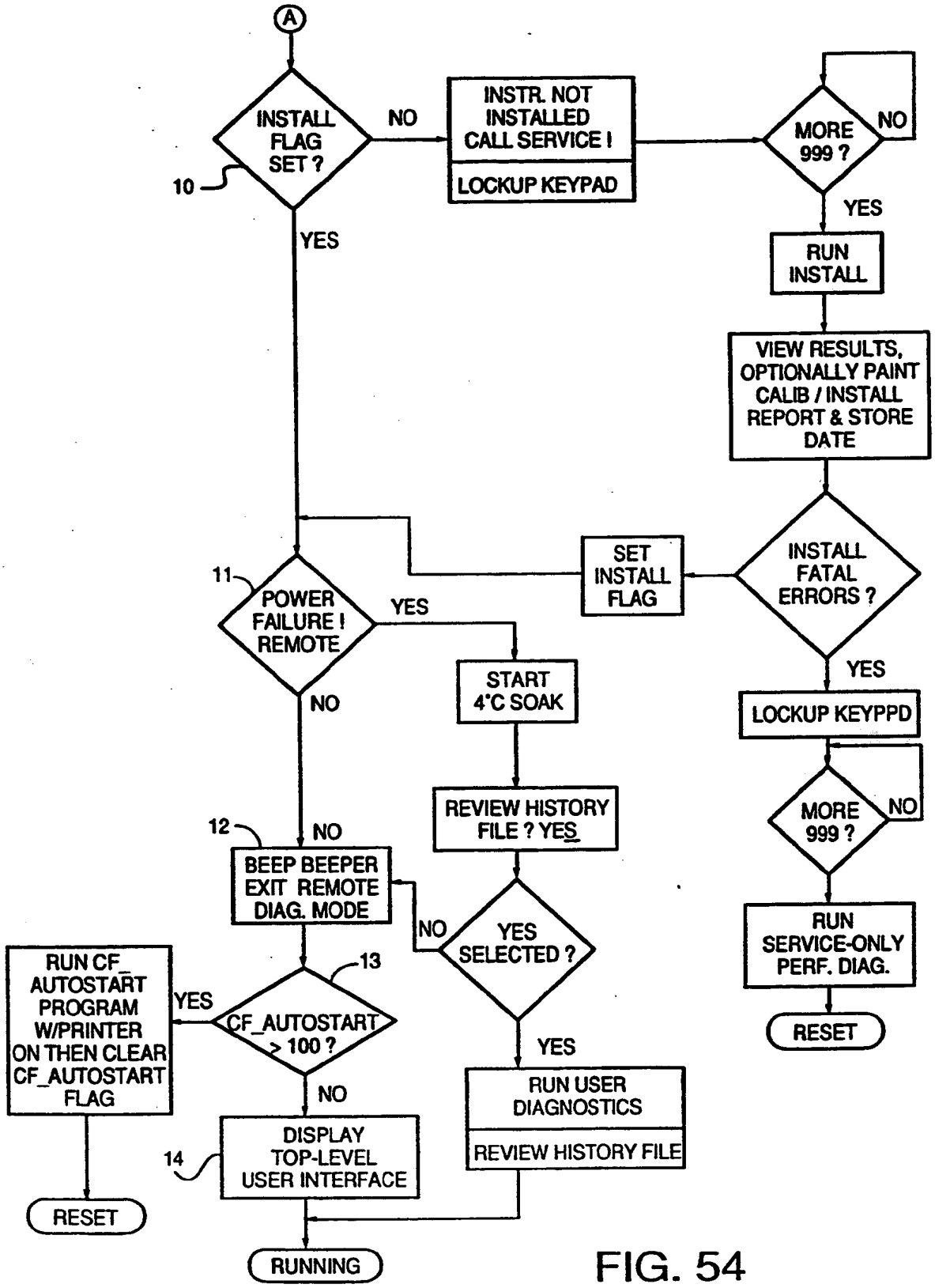

FIG. 54

BNSDOCID: <EP___0810030A1_I_>

European Patent Office

EUROPEAN SEARCH REPORT

Application Number
EP 97 11 2541

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
Y	EP 0 388 159 A (SEIKO INSTR INC) 19 September 1990 * column 1, line 6 - line 36; figures 2,4 * ---	1,5	B01L7/00 B01L3/00 B01L9/06 C12Q1/68 G05D23/19
Y	DE 26 03 683 A (LOO HANS MICHAEL VAN DE DR RER) 11 August 1977 * page 2, line 1 - line 17 * * page 2, line 26 - page 3, line 33; figures * ---	1,5	
A	EP 0 311 440 A (SEIKO INSTR INC) 12 April 1989 * the whole document * ---	1,5	
A	US 3 483 997 A (RITTER HARRY W) 16 December 1969 * the whole document * ---	1,5,9	
X	DE 88 08 738 U (DIEKMANN) 1 September 1988 * page 3, line 4 - line 26 * * page 5, line 8 - line 20; figure * -----	6-11	

TECHNICAL FIELDS SEARCHED (Int.Cl.6)
B01L

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	11 September 1997	Hocquet, A

CATEGORY OF CITED DOCUMENTS

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